jc685 U.S. PTO
11/06/00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
REQUEST FOR FILING APPLICATION UNDER RULE 1.53(b)

jc813 U.S. PTO
09/705911
11/06/00

Pursuant to 37 CFR 1.53(b), please file a ☐ continuation/☒ divisional of the pending prior PATENT APPLICATION of:
Inventor: HERMON-TAYLOR et al.
Serial No. 09/091,538
Filed: September 16, 1998
For: NOVEL POLYNUCLEOTIDES AND POLYPEPTIDES IN PATHOGENIC MYCOBACTERIA AND THEIR USE AS DIAGNOSTICS, VACCINES AND TARGETS FOR CHEMOTHERAPY

Atty Dkt.: 117-323
C# M#
Date: November 6, 2000
Group: 1645
Examiner: R. Baskar

Assistant Commissioner for Patents
Washington, DC 20231
Sir:

This request for filing under Rule 53(b) is made by the following named inventor(s) (using the above-identified title):
Inventor(s): HERMON-TAYLOR et al.

☒ Attached is a true copy of the prior application as originally filed including the specification, claims, Oath/Declaration and drawings (if any) and abstract (if any). No amendments (if any) referenced in the Oath or Declaration filed to complete the prior application introduced new matter.

☒ Priority is hereby claimed under 35 USC 119 based on the following foreign applications, the entire content of which is hereby incorporated by reference in this application:

Application Number	Country	Day/Month/Year/Filed
9526178.0	Great Britain	21 December 1995
PCT/GB96/03221	PCT	23 December 1996

☒ certified copy(ies) of foreign application(s) attached or
☐ already filed on _____ in prior appln. no. _____ filed _____
☒ already filed in 09/091,538 filed Septemer 16, 1998

☐ Please amend the specification by inserting before the first line: -- This application claims the benefit of U.S. Provisional Application No. , filed , the entire content of which is hereby incorporated by reference in this application.--

☒ The prior application is assigned to St. George's Hospital Medical School.

☒ Power of Attorney has been granted to B.J. Sadoff et al, Reg. No. 36,663 of Nixon & Vanderhye P.C., 1100 N. Glebe Rd., 8th Floor, Arlington, VA 22201.

☒ Address all future communications to: Nixon & Vanderhye P.C., 1100 N. Glebe Rd., 8th Floor, Arlington, VA 22201.

☒ Please amend the specification by inserting before the first line --This is a divisional of application Serial No. 09/091,538, filed September 16, 1998, now pending, which is a 371 application of PCT/GB96/03221, filed December 23, 1996 the entire content of which is hereby incorporated by reference in this application.--

☐ "Small entity" statement of record. ☐ "Small entity" statement attached.

☐ Petition filed in prior application to extend its life to insure co-pendency.

☒ The Examiner's attention is directed to the prior art cited in the parent application by applicant and/or Examiner for the reasons stated therein.

☒ Please enter the attached and/or below preliminary amendment **prior** to calculation of filing fee:

☒ The entire disclosure of the prior application above-referenced is considered as being part of the disclosure of this new application and is hereby incorporated by reference therein.

FILING FEE IS BASED ON CLAIMS AS FILED LESS ANY HEREWITH CANCELED

Basic Filing Fee					$	710.00
Total effective claims	23	- 20 (at least 20) =	3	x $ 18.00	$	54.00
Independent claims	4	- 3 (at least 3) =	1	x $ 80.00	$	80.00
If any proper multiple dependent claims now added for first time, add $270.00 (ignore improper)					$	270.00
				SUBTOTAL	$	1,114.00
If "small entity," then enter half (1/2) of subtotal and subtract					-$(	0.00)
				SECOND SUBTOTAL	$	1,114.00
Assignment Recording Fee ($40.00)					$	0.00
				TOTAL FEE ENCLOSED	$	1,114.00

Any future submission requiring an extension of time is hereby stated to include a petition for such time extension. The Commissioner is hereby authorized to charge any deficiency in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Account No. 14-1140.** A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: B.J. Sadoff, Reg. No. 36,663

Signature: _____

472678

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

HERMON-TAYLOR et al.

Atty. Ref.: 117-323

Divisional of Serial No. 09/091,538

Group: Unassigned

Filed: Herewith

Examiner: Unassigned

For: NOVEL POLYNUCLEOTIDES AND POLYPEPTIDES IN PATHOGENIC MYCOBACTERIA AND THEIR USE AS DIAGNOSTICS, VACCINES AND TARGETS FOR CHEMOTHERAPY

* * * * * * * * * * *

November 6, 2000

Assistant Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Sir:

Entry and consideration of the following amendments and remarks are requested.

IN THE SPECIFICATION:

Amend the specification as follows.

Insert the attached Sequence Listing after the claims pages.

IN THE CLAIMS:

Amend the claims as follows.

Cancel claims 2, 3, 16 and 17, without prejudice.

4. (Amended) A polynucleotide in substantially isolated form which encodes a polypeptide according to claim 1 [any one of claims 1 to 3].

8. (Amended) A polynucleotide probe which comprises a fragment of at least 15 nucleotides of a polynucleotide as defined in claim 5 [any one of claims 4 to 7], optionally carrying a revealing label.

9. (Amended) A recombinant vector carrying a polynucleotide as defined in claim 5 [any one of claims 4 to 7].

10. (Amended) An antibody capable of binding a polypeptide or fragment thereof as defined in claim 1 [any one of claims 1 to 3].

12. (Amended) A test kit for detecting the presence or absence of a pathogenic mycobacterium in a sample which comprises a polynucleotide according to claim 4 [any one of claims 4 to 8], a polypeptide according to claim 1 [any one of claims 1 to 3], a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, or an antibody according to claim 10 [, any one of claims 10 or 11].

13. (Amended) A method of detecting the presence or absence of antibodies in an animal or human, against a pathogenic mycobacteria in a sample which comprises:

(a) providing a polypeptide according to [any one of claims 1 to 3] claim 1 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which comprises an epitope;

(b) incubating a biological sample with said polypeptide under conditions which allow for the formation of an antibody—antigen complex; and

(c) determining whether antibody-antigen complex comprising said polypeptide is formed.

14. (Amended) A method of detecting the presence or absence of a polypeptide according to [any one of claims 1 to 3] claim 1 or a polypeptide which comprises a sequence

selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto in a biological sample which method which comprises:

(a) providing an antibody according to claim 10 [any one of claims 10 and 11];

(b) incubating a biological sample with said antibody under conditions which allow for the formation of an antibody-antigen complex; and

(c) determining whether antibody-antigen complex comprising said antibody is formed.

15. (Amended) A method of detecting the presence or absence of cell mediated immune reactivity in an animal or human, to a polypeptide according to claim 1 [claims 1 to 3] or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which method comprises

(a) providing a polypeptide according to claim 1 [any one of claims 1 to 3] or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which comprises an epitope;

(b) incubating a cell sample with said polypeptide under conditions which allow for a cellular immune response such as release of cytokines or other mediator or reaction to occur; and

(c) detecting the presence of said cytokine or mediator or cellular response in the incubate.

18. (Amended) A method of treating or preventing mycobacterial disease in an animal or human caused by mycobacteria which express a polypeptide according to [claims 1 to 3] claim 1 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which method comprises vaccinating or treating an animal or human with an effective amount of said polypeptide.

19. (Amended) A method of treating or preventing mycobacterial diseases in animals or humans caused by mycobacteria containing the polynucleotide of Seq.ID.No: 3 or 4, which method comprises vaccinating or treating an animal or human with an effective amount of a polynucleotide according to claim 4 [claims 4 to 7], a vector according to claim 9 or a polynucleotide which encodes a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto.

20. (Amended) A method according to claim 18 [claims 18 or 19] for increasing the in vivo susceptibility of mycobacteria to antimicrobial drugs.

21. (Amended) A normally pathogenic mycobacterium, whose pathogenicity is mediated in all or in part by the presence or the expression of a polypeptide as defined in [any one of claims 1 to 3] claim 1 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which mycobacterium harbours an attenuating mutation in a gene encoding one of the said polypeptides.

REMARKS

The claims have been amended to reduce the filing fees and delete improper multiple dependencies.

The specification has been amended to include a Sequence Listing, a copy of which was filed in the parent Application No.09/091,538. The attached paper copy of the Sequence Listing is the same as the paper and computer readable copies of the Sequence Listing submitted in Application No. 09/091,538. The Office is requested to use the computer readable form of the Sequence Listing in the parent Application No. 09/091,538, in the present application. A separate Request to this effect is attached. No new matter has been added.

An early and favorable Action on the merits is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

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Novel polynucleotides and polypeptides in pathogenic mycobacteria and their use as diagnostics, vaccines and targets for chemotherapy.

This invention relates to the novel polynucleotide sequence we have designated "GS" which we have identified in pathogenic mycobacteria. GS is a pathogenicity island within 8kb of DNA comprising a core region of 5.75kb and an adjacent transmissable element within 2.25kb. GS is contained within *Mycobacterium paratuberculosis, Mycobacterium avium* subsp. *silvaticum* and some pathogenic isolates of *M.avium*. Functional portions of the core region of GS are also represented by regions with a high degree of homology that we have identified in cosmids containing genomic DNA from *Mycobacterium tuberculosis*.

Background to the invention

Mycobacterium tuberculosis (Mtb) is a major cause of global diseases of humans as well as animals. Although conventional methods of diagnosis including microscopy, culture and skin testing exist for the recognition of these diseases, improved methods particularly new immunodiagnostics and DNA-based detection systems are needed. Drugs used to treat tuberculosis are increasingly encountering the problem of resistant organisms. New drugs targeted at specific pathogenicity determinants as well as new vaccines for the prevention and treatment of tuberculosis are required. The importance of *Mtb* as a global pathogen is reflected in the commitment being made to sequencing the entire genome of this organism. This has generated a large amount of DNA sequence data of genomic DNA within cosmid and other libraries. Although the DNA sequence is known in the art, the functions of the vast majority of these sequences, the proteins they encode, the biological significance of these proteins, and the overall relevance and use of these genes and their products as diagnostics, vaccines and targets for chemotherapy for tuberculous disease, remains entirely unknown.

Mycobacterium avium subsp.*silvaticum (Mavs)* is a pathogenic mycobacterium causing diseases of animals and birds, but it can

also affect humans. *Mycobacterium paratuberculosis* (*Mptb*) causes chronic inflammation of the intestine in many species of animals including primates and can also cause Crohn's disease in humans. *Mptb* is associated with other chronic inflammatory diseases of humans such as sarcoidosis. Subclinical *Mptb* infection is widespread in domestic livestock and is present in milk from infected animals. The organism is more resistant to pasteurisation than *Mtb* and can be conveyed to humans in retail milk supplies. *Mptb* is also present in water supplies, particularly those contaminated with run-off from heavily grazed pastures. *Mptb* and *Mavs* contain the insertion elements *IS900* and *IS902* respectively, and these are linked to pathogenicity in these organisms. *IS900* and *IS902* provide convenient highly specific multi-copy DNA targets for the sensitive detection of these organisms using DNA-based methods and for the diagnosis of infections in animals and humans. Much improvement is however required in the immunodiagnosis of *Mptb* and *Mavs* infections in animals and humans. *Mptb* and *Mavs* are in general, resistant in vivo to standard anti-tuberculous drugs. Although substantial clinical improvements in infections caused by *Mptb*, such as Crohn's disease, may result from treatment of patients with combinations of existing drugs such as Rifabutin, Clarithromycin or Azithromycin, additional effective drug treatments are required. Furthermore, there is an urgent need for effective vaccines for the prevention and treatment of *Mptb* and *Mavs* infections in animals and humans based upon the recognition of specific pathogenicity determinants.

Pathogenicity islands are, in general, 7-9kb regions of DNA comprising a core domain with multiple ORFs and an adjacent transmissable element. The transmissable element also encodes proteins which may be linked to pathogenicity, such as by providing receptors for cellular recognition. Pathogenicity islands are envisaged as mobile packages of DNA which, when they enter an organism, assist in bringing about its convertion from a non-disease-causing to a disease-causing strain.

Description of the Drawings

Figure 1(a) and (b) shows a linear map of the pathogenicity island GS in *Mavs* (Fig 1a) and in *Mptb* (Fig 1b). The main open reading frames are illustrated as ORFs A to H. ORFs A to F are found within the core region of GS. ORFs G and H are encoded by the adjacent transmissable element portion of GS.

Disclosure of the invention

Using a DNA-based differential analysis technology we have discovered and characterised a novel polynucleotide in *Mptb* (isolates 0022 from a Guernsey cow and 0021 from a red deer). This polynucleotide comprises the gene region we have designated GS. GS is found in *Mptb* using the identifier DNA sequences Seq.ID.No 1 and 2 where the Seq.ID No2 is the complementary sequence of Seq.ID No 1. GS is also identified in *Mavs*. The complete DNA sequence incorporating the positive strand of GS from an isolate of *Mavs* comprising 7995 nucleotides, including the core region of GS and adjacent transsmissable element, is given in Seq.ID No.3. DNA sequence comprising 4435 bp of the positive strand of GS obtained from an isolate of *Mptb* including the core region of GS (nucleotides 1614 to 6047 of GS in *Mavs*) is given in Seq.ID No 4. The DNA sequence of GS from *Mptb* is highly (99.4%) homologous to GS in *Mavs*. The remaining portion of the DNA sequence of GS in *Mptb*, is readily obtainable by a person skilled in the art using standard laboratory procedures. The entire functional DNA sequence including core region and transmisable element of GS in *Mptb* and *Mavs* as described above, comprise the polynucleotide sequences of the invention.

There are 8 open reading frames (ORFs) in GS. Six of these designated GSA, GSB, GSC, GSD, GSE and GSF are encoded by the core DNA region of GS which, characteristically for a pathogenicity island, has a different GC content than the rest of the microbial genome. Two ORFs designated GSG and GSH are encoded by the transmissable element of GS whose GC content resembles that of the rest of the mycobacterial genome. The ORF GSH comprises two sub-ORFs H_1 H_2 on the complementary DNA strand linked by a programmed frameshifting site so that a single polypeptide is translated from the ORF GSH. The nucleotide

sequences of the 8 ORFs in GS and their translations are shown in Seq. ID No 5 to Seq.ID No 29 as follows:

ORF A: Seq. ID No 5 Nucleotides 50 to 427 of GS from *Mavs*
Seq. ID No 6 Amino acid sequence encoded by Seq.ID No 5.

ORF B: Seq. ID No 7 Nucleotides 772 to 1605 of GS from *Mavs*
Seq. ID No 8 Amino acid sequence encoded by Seq.ID No 7.

ORF C: Seq. ID No 9 Nucleotides 1814 to 2845 of GS from *Mavs*
Seq. ID No 10 Amino acid sequence encoded by Seq.ID No 9.
Seq. ID No 11 Nucleotides 201 to 1232 of GS from *Mptb*
Seq. ID No 12 Amino acid sequence encoded by Seq.ID No 11

ORF D: Seq. ID No 13 Nucleotides 2785 to 3804 of GS from *Mavs*
Seq. ID No 14 Amino acid sequence encoded by Seq.ID No 13.
Seq. ID No 15 Nucleotides 1172 to 2191 of GS from *Mptb*
Seq. ID No 16 Amino acid sequence encoded by Seq.ID No 15.

ORF E: Seq. ID No 17 Nucleotides 4080 to 4802 of GS from *Mavs*
Seq. ID No 18 Amino acid sequence encoded by Seq.ID No 17.
Seq. ID No 19 Nucleotides 2467 to 3189 of GS from *Mptb*
Seq. ID No 20 Amino acid sequence encoded by Seq.ID No 19.

ORF F: Seq. ID No 21 Nucleotides 4947 to 5747 of GS from *Mavs*
Seq. ID No 22 Amino acid sequence encoded by Seq.ID No 21.
Seq. ID No 23 Nucleotides 3335 to 4135 of GS from *Mptb*
Seq. ID No 24 Amino acid sequence encoded by Seq.ID No 23.

ORF G: Seq. ID No 25 Nucleotides 6176 to 7042 of GS from *Mavs*
Seq. ID No 26 Amino acid sequence encoded by Seq.ID No 25.

ORF H: Seq.ID No 27 Nucleotides 7953 to 6215 from *Mavs*.

ORF H_1: Seq.ID No 28 Amino acid sequence encoded by nucleotides 7953 to 7006 of Seq.ID No 27

ORF H_2: Seq.ID No 29 Amino acid sequence encoded by nucleotides 7009 to 6215 of Seq.ID No 27

The polynucleotides in *Mtb* with homology to the ORFs B, C, E and F of GS in *Mptb* and *Mavs*, and the polypeptides they are now known to encode as a result of our invention, are as follows:

ORF B: Seq.ID No 30 Cosmid MTCY277 nucleotides 35493 to 34705
Seq.ID No 31 Amino acid sequence encoded by Seq.ID No30.

ORF C: Seq.ID No 32 Cosmid MTCY277 nucleotides 31972 to 32994
Seq.ID No 33 Amino acid sequence encoded by Seq.ID No32.

ORF E: Seq.ID No 34 Cosmid MTCY277 nucleotides 34687 to 33956
Seq.ID No 35 Amino acid sequence encoded by Seq.ID No34.

ORF E: Seq.ID No 36 Cosmid MTO24 nucleotides 15934 to 15203
Seq.ID No 37 Amino acid sequence encoded by Seq.ID No36.

ORF F: Seq.ID No38 Cosmid MTO24 nucleotides 15133 to 14306
Seq.ID No 39 Amino acid sequence encoded by Seq.ID No38.

The proteins and peptides encoded by the ORFs A to H in *Mptb* and *Mavs* and the amino acid sequences from homologous genes we have

discovered in *Mtb* given in Seq.ID Nos 31, 33, 35, 37 and 39, as described above and fragments thereof, comprise the polypeptides of the invention. The polypeptides of the invention are believed to be associated with specific immunoreactivity and with the pathogenicity of the host micro-organisms from which they were obtained.

The present invention thus provides a polynucleotide in substantially isolated form which is capable of selectively hybridising to sequence ID Nos 3 or 4 or a fragment thereof. The polynucleotide fragment may alternatively comprise a sequence selected from the group of Seq.ID.No: 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and 27. The invention further provides a polynucleotide in substantially isolated form whose sequence consists essentially of a sequence selected from the group Seq ID Nos. 30, 32, 34, 36 and 38, or a corresponding sequence selectively hybridizable thereto, or a fragment of said sequence or corresponding sequence.

The invention further provides diagnostic probes such as a probe which comprises a fragment of at least 15 nucleotides of a polynucleotide of the invention, or a peptide nucleic acid or similar synthetic sequence specific ligand, optionally carrying a revealing label. The invention also provides a vector carrying a polynucleotide as defined above, particularly an expression vector.

The invention further provides a polypeptide in substantially isolated form which comprises any one of the sequences selected from the group consisting Seq.ID.No: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 29, 31, 33, 35, 37 and 39, or a polypeptide substantially homologous thereto. The invention additionally provides a polypeptide fragment which comprises a fragment of a polypeptide defined above, said fragment comprising at least 10 amino acids and an epitope. The invention also provides polynucleotides in substantially isolated form which encode polypeptides of the invention, and vectors which comprise such polynucleotides, as well as antibodies capable of binding such polypeptides. In an additional aspect, the invention provides

kits comprising polynucleotides, polypeptides, antibodies or synthetic ligands of the invention and methods of using such kits in diagnosing the presence or absence of mycobacteria in a sample. The invention also provides pharmaceutical compositions comprising polynucleotides of the invention, polypeptides of the invention or antisense probes and the use of such compositions in the treatment or prevention of diseases caused by mycobacteria. The invention also provides polynucleotihe prevention and treatment of infections due to GS-containing pathogenic mycobacteria in animals and humans and as a means of enhacing in vivo susceptibility of said mycobacteria to antimicrobial drugs. The invention also provides bacteria or viruses transformed with polynucleotides of the invention for use as vaccines. The invention further provides *Mptb* or *Mavs* in which all or part or the polynucleotides of the invention have been deleted or disabled to provide mutated organisms of lower pathogenicity for use as vaccines in animals and humans. The invention further provides *Mtb* in which all or part of the polynucleotides encoding polypeptides of the invention have been deleted or disabled to provided mutated organisms or lower pathogenicity for use as vaccines in animals and humans.

A further aspect of the invention is our discovery of homologies between the ORFs B, C and E in GS on the one hand, and *Mtb* cosmid MTCY277 on the other (data from Genbank database using the computer programmes BLAST and BLIXEM). The homologous ORFs in MTCY277 are adjacent to one another consistent with the form of another pathogenicity island in *Mtb*. A further aspect of the invention is our discovery of homologies between ORFs E and F in GS, and *Mtb* cosmid MTO24 (also Genbank, as above) with the homologous ORFs close to one another. The use of polynucleotides and polypeptides from *Mtb* (Seq. ID Nos 30,31, 32, 33, 34, 35, 36, 37, 38 and 39) in substantially isolated form as diagnostics, vaccines and targets for chemotherapy, for the management and prevention of *Mtb* infections in humans and animals, and the processes involved in the preparation and use of these diagnostics, vaccines and new chemotherapeutic agents, comprise further aspects of the invention.

Detailed description of the invention.

A. Polynucleotides

Polynucleotides of the invention as defined herein may comprise DNA or RNA. They may also be polynucleotides which include within them synthetic or modified nucleotides or peptide nucleic acids. A number of different types of modification to oligonucleotides are known in the art. These include methylphosphonate and phosphorothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. For the purposes of the present invention, it is to be understood that the polynucleotides described herein may be modified by any method available in the art. Such modifications may be carried out in order to couple the said polynucleotide to a solid phase or to enhance the recognition, the *in vivo* activity, or the lifespan of polynucleotides of the invention.

A number of different types of polynucleotides of the invention are envisaged. In the broadest aspect, polynucleotides and fragments thereof capable of hybridizing to SEQ ID NO:3 or 4 form a first aspect of the invention. This includes the polynucleotide of SEQ ID NO: 3 or 4. Within this class of polynucleotides various sub-classes of polynucleotides are of particular interest.

One sub-class of polynucleotides which is of interest is the class of polynucleotides encoding the open reading frames A, B, C, D, E, F, G and H, including SEQ ID NOs:5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and 27. As discussed below, polynucleotides encoding ORF H include the polynucleotide sequences 7953 to 7006 and 7009 to 6215 within SEQ ID NO: 27, as well as modified sequences in which the frame-shift has been modified so that the two sub-reading frames are placed in a single reading frame. This may be desirable where the polypeptide is to be produced in recombinant expression systems.

The invention thus provides a polynucleotide in substantially isolated form which encodes any one of these ORFs or combinations

thereof. Combinations thereof includes combinations of 2, 3, 4, 5 or all of the ORFs. Polynucleotides may be provided which comprise an individual ORF carried in a recombinant vector including the vectors described herein. Thus in one preferred aspect the invention provides a polynucleotide in substantially isolated form capable of selectively hybridizing to the nucleic acid comprising ORFs A to F of the core region of the *Mptb* and *Mavs* pathogenicity islands of the invention. Fragments thereof corresponding to ORFs A to E, B to F, A to D, B to E, A to C, B to D or any two adjacent ORFs are also included in the invention.

Polynucleotides of the invention will be capable of selectively hybridizing to the corresponding portion of the GS region, or to the corresponding ORFs of *Mtb* described herein. The term "selectively hybridizing" indicates that the polynucleotides will hybridize, under conditions of medium to high stringency (for example 0.03 M sodium chloride and 0.03 M sodium citrate at from about 50°C to about 60°C) to the corresponding portion of SEQ ID NO:3 or 4 or the complementary strands thereof but not to genomic DNA from mycobacteria which are usually non-pathogenic including non-pathogenic species of *M.avium*. Such polynucleotides will generally be generally at least 68%, e.g. at least 70%, preferably at least 80 or 90% and more preferably at least 95% homologous to the corresponding DNA of GS. The corresponding portion will be of over a region of at least 20, preferably at least 30, for instance at least 40, 60 or 100 or more contiguous nucleotides.

By "corresponding portion" it is meant a sequence from the GS region of the same or substantially similar size which has been determined, for example by computer alignment, to have the greatest degree of homology to the polynucleotide.

Any combination of the above mentioned degrees of homology and minimum sizes may be used to define polynucleotides of the invention, with the more stringent combinations (i.e. higher homology over longer lengths) being preferred. Thus for example a polynucleotide which is at least 80% homologous over 25, preferably 30 nucleotides forms one aspect of the invention, as

does a polynucleotide which is at least 90% homologous over 40 nucleotides.

A further class of polynucleotides of the invention is the class of polynucleotides encoding polypeptides of the invention, the polypeptides of the invention being defined in section B below. Due to the redundancy of the genetic code as such, polynucleotides may be of a lower degree of homology than required for selective hybridization to the GS region. However, when such polynucleotides encode polypeptides of the invention these polynucleotides form a further aspect. It may for example be desirable where polypeptides of the invention are produced recombinantly to increase the GC content of such polynucleotides. This increase in GC content may result in higher levels of expression via codon usage more appropriate to the host cell in which recombinant expression is taking place.

An additional class of polynucleotides of the invention are those obtainable from cosmids MTCY277 and MT024 (containing *Mtb* genomic sequences), which polynucleotides consist essentially of the fragment of the cosmid containing an open reading frame encoding any one of the homologous ORFs B, C, E or F respectively. Such polynucleotides are referred to below as *Mtb* polynucleotides. However, where reference is made to polynucleotides in general such reference includes *Mtb* polynucleotides unless the context is explicitly to the contrary. In addition, the invention provides polynucleotides which encode the same polypeptide as the abovementioned ORFs of *Mtb* but which, due to the redundancy of the genetic code, have different nucleotide sequences. These form further *Mtb* polynucleotides of the invention. Fragments of *Mtb* polynucleotides suitable for use as probes or primers also form a further aspect of the invention.

The invention further provides polynucleotides in substantially isolated form capable of selectively hybridizing (where selectively hybridizing is as defined above) to the *Mtb* polynucleotides of the invention.

The invention further provides the *Mtb* polynucleotides of the invention linked, at either the 5' and/or 3' end to polynucleotide sequences to which they are not naturally contiguous. Such sequences will typically be sequences found in cloning or expression vectors, such as promoters, 5' untranslated sequence, 3' untranslated sequence or termination sequences. The sequences may also include further coding sequences such as signal sequences used in recombinant production of proteins.

Further polynucleotides of the invention are illustrated in the accompanying examples.

Polynucleotides of the invention may be used to produce a primer, e.g. a PCR primer, a primer for an alternative amplification reaction, a probe e.g. labelled with a revealing label by conventional means using radioactive or non-radioactive labels or a probe linked covalently to a solid phase, or the polynucleotides may be cloned into vectors. Such primers, probes and other fragments will be at least 15, preferably at least 20, for example at least 25, 30 or 40 or more nucleotides in length, and are also encompassed by the term polynucleotides of the invention as used herein.

Primers of the invention which are preferred include primers directed to any part of the ORFs defined herein. The ORFs from other isolates of pathogenic mycobacteria which contain a GS region may be determined and conserved regions within each individual ORF may be identified. Primers directed to such conserved regions form a further preferred aspect of the invention. In addition, the primers and other polynucleotides of the invention may be used to identify, obtain and isolate ORFs capable of selectively hybridizing to the polynucleotides of the invention which are present in pathogenic mycobacteria but which are not part of a pathogenicity island in that particular species of bacteria. Thus in addition to the ORFs B, C, E and F which have been identified in *Mtb*, similar ORFs may be identified in other pathogens and ORFs corresponding to the GS ORFs C, D, E, F and H, may also be identified.

Polynucleotides such as DNA polynucleotides and probes according to the invention may be produced recombinantly, synthetically, or by any means available to those of skill in the art. They may also be cloned by standard techniques.

In general, primers will be produced by synthetic means, involving a step-wise manufacture of the desired nucleic acid sequence one nucleotide at a time. Techniques for accomplishing this using automated techniques are readily available in the art. Longer polynucleotides will generally be produced using recombinant means, for example using a PCR (polymerase chain reaction) cloning techniques. This will involve making a pair or primers (e.g. of about 15-30 nucleotides) to a region of GS, which it is desired to clone, bringing the primers into contact with genomic DNA from a mycobacterium or a vector carrying the GS sequence, performing a polymerase chain reaction under conditions which bring about amplification of the desired region, isolating the amplified fragment (e.g. by purifying the reaction mixture on an agarose gel) and recovering the amplified DNA. The primers may be designed to contain suitable restriction enzyme recognition sites so that the amplified DNA can be cloned into a suitable cloning vector.

Such techniques may be used to obtain all or part of the GS or ORF sequences described herein, as well as further genomic clones containing full open reading frames. Although in general such techniques are well known in the art, reference may be made in particular to Sambrook J., Fritsch EF., Maniatis T (1989). Molecular cloning: a Laboratory Manual, 2nd edn. Cold Spring Harbor, New York, Cold Spring Harbor Laboratory.

Polynucleotides which are not 100% homologous to the sequences of the present invention but fall within the scope of the invention can be obtained in a number of ways.

Other isolates or strains of pathogenic mycobacteria will be expected to contain allelic variants of the GS sequences described herein, and these may be obtained for example by probing genomic DNA libraries made from such isolates or strains

of bacteria using GS or ORF sequences as probes under conditions of medium to high stringency (for example 0.03M sodium chloride and 0.03M sodium citrate at from about 50°C to about 60°C).

A particularly preferred group of pathogenic mycobacteria are isolates of *M.paratuberculosis*. Polynucleotides based on GS regions from such bacteria are particularly preferred. Preferred fragments of such regions include fragments encoding individual open reading frames including the preferred groups and combinations of open reading frames discussed above.

Alternatively, such polynucleotides may be obtained by site directed mutagenesis of the GS or ORF sequences or allelic variants thereof. This may be useful where for example silent codon changes are required to sequences to optimise codon preferences for a particular host cell in which the polynucleotide sequences are being expressed. Other sequence changes may be desired in order to introduce restriction enzyme recognition sites, or to alter the property or function of the polypeptides encoded by the polynucleotides of the invention. Such altered property or function will include the addition of amino acid sequences of consensus signal peptides known in the art to effect transport and secretion of the modified polypeptide of the invention. Another altered property will include metagenesis of a catalytic residue or generation of fusion proteins with another polypeptide. Such fusion proteins may be with an enzyme, with an antibody or with a cytokine or other ligand for a receptor, to target a polypeptide of the invention to a specific cell type *in vitro* or *in vivo*.

The invention further provides double stranded polynucleotides comprising a polynucleotide of the invention and its complement.

Polynucleotides or primers of the invention may carry a revealing label. Suitable labels include radioisotopes such as ^{32}P or ^{35}S, enzyme labels, other protein labels or smaller labels such as biotin or fluorophores. Such labels may be added to polynucleotides or primers of the invention and may be detected using by techniques known per se.

Polynucleotides or primers of the invention or fragments thereof labelled or unlabelled may be used by a person skilled in the art in nucleic acid-based tests for the presence or absence of *Mptb*, *Mavs*, other GS-containing pathogenic mycobacteria, or *Mtb* applied to samples of body fluids, tissues, or excreta from animals and humans, as well as to food and environmental samples such as river or ground water and domestic water supplies.

Human and animal body fluids include sputum, blood, serum, plasma, saliva, milk, urine, csf, semen, faeces and infected discharges. Tissues include intestine, mouth ulcers, skin, lymph nodes, spleen, lung and liver obtained surgically or by a biopsy technique. Animals particularly include commercial livestock such as cattle, sheep, goats, deer, rabbits but wild animals and animals in zoos may also be tested.

Such tests comprise bringing a human or animal body fluid or tissue extract, or an extract of an environmental or food sample, into contact with a probe comprising a polynucleotide or primer of the invention under hybridising conditions and detecting any duplex formed between the probe and nucleic acid in the sample. Such detection may be achieved using techniques such as PCR or by immobilising the probe on a solid support, removing nucleic acid in the sample which is not hybridized to the probe, and then detecting nucleic acid which has hybridized to the probe. Alternatively, the sample nucleic acid may be immobilized on a solid support, and the amount of probe bound to such a support can be detected. Suitable assay methods of this any other formats can be found in for example WO89/03891 and WO90/13667.

Polynucleotides of the invention or fragments thereof labelled or unlabelled may also be used to identify and characterise different strains of *Mptb*, *Mavs*, other GS-containing pathogenic mycobacteria, or *Mtb*, and properties such as drug resistance or susceptibility.

The probes of the invention may conveniently be packaged in the form of a test kit in a suitable container. In such kits the probe may be bound to a solid support where the assay format for

which the kit is designed requires such binding. The kit may also contain suitable reagents for treating the sample to be probed, hybridising the probe to nucleic acid in the sample, control reagents, instructions, and the like.

The use of polynucleotides of the invention in the diagnosis of inflammatory diseases such as Crohn's disease or sarcoidosis in humans or Johne's disease in animals form a preferred aspect of the invention. The polynucleotides may also be used in the prognosis of these diseases. For example, the response of a human or animal subject in response to antibiotic, vaccination or other therapies may be monitored by utilizing the diagnostic methods of the invention over the course of a period of treatment and following such treatment.

The use of *Mtb* polynucleotides (particularly in the form of probes and primers) of the invention in the above-described methods form a further aspect of the invention, particularly for the detection, diagnosis or prognosis of *Mtb* infections.

B. Polypeptides.

Polypeptides of the invention include polypeptides in substantially isolated form encoded by GS. This includes the full length polypeptides encoded by the positive and complementary negative strands of GS. Each of the full length polypeptides will contain one of the amino acid sequences set out in Seq ID NOs:6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28 and 29. Polypeptides of the invention further include variants of such sequences, including naturally occurring allelic variants and synthetic variants which are substantially homologous to said polypeptides. In this context, substantial homology is regarded as a sequence which has at least 70%, e.g. 80%, 90%, 95% or 98% amino acid homology (identity) over 30 or more, e.g 40, 50 or 100 amino acids. For example, one group of substantially homolgous polypeptides are those which have at least 95% amino acid identity to a polypeptide of any one of Seq ID NOs:6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28 and 29 over their entire length. Even more preferably, this homology is 98%.

Polypeptides of the invention further include the polypeptide sequences of the homologous ORFs of *Mtb*, namely Seq ID Nos. 31, 33, 35, 37 and 39. Unless explicitly specified to the contrary, reference to polypeptides of the invention and their fragments include these *Mtb* polypeptides and fragments, and variants thereof (substanially homologous to said sequences) as defined herein.

Polypeptides of the invention may be obtained by the standard techniques mentioned above. Polypeptides of the invention also include fragments of the above mentioned full length polypeptides and variants thereof, including fragments of the sequences set out in SEQ ID NOs:6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 29, 31, 33, 35, 37 and 39. Such fragments for example of 8, 10, 12, 15 or up to 30 or 40 amino acids may also be obtained synthetically using standard techniques known in the art.

Preferred fragments include those which include an epitope, especially an epitope which is specific to the pathogenicity of the mycobacterial cell from which the polypeptide is derived. Suitable fragments will be at least about 5, e.g. 8, 10, 12, 15 or 20 amino acids in size, or larger. Epitopes may be determined either by techniques such as peptide scanning techniques as described by Geysen et al, Mol.Immunol., 23; 709-715 (1986), as well as other techniques known in the art.

The term "an epitope which is specific to the pathogenicity of the mycobacterial cell" means that the epitope is encoded by a portion of the GS region, or by the corresponding ORF sequences of *Mtb* which can be used to distinguish mycobacteria which are pathogenic by from related non-pathogenic mycobacteria including non-pathogenic species of *M.avium*. This may be determined using routine methodology. A candidate epitope from an ORF may be prepared and used to immunise an animal such as a rat or rabbit in order to generate antibodies. The antibodies may then be used to detect the presence of the epitope in pathogenic mycobacteria and to confirm that non-pathogenic mycobacteria do not contain any proteins which react with the epitope. Epitopes may be linear or conformational.

Polypeptides of the invention may be in a substantially isolated form. It will be understood that the polypeptide may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide of the invention may also be in a substantially purified form, in which case it will generally comprise the polypeptide in a preparation in which more than 90%, e.g. 95%, 98% or 99% of the polypeptide in the preparation is a polypeptide of the invention.

Polypeptides of the invention may be modified to confer a desired property or function for example by the addition of Histidine residues to assist their purification or by the addition of a signal sequence to promote their secretion from a cell.

Thus, polypeptides of the invention include fusion proteins which comprise a polypeptide encoding all or part of one or more of an ORF of the invention fused at the N- or C-terminus to a second sequence to provide the desired property or function. Sequences which promote secretion from a cell include, for example the yeast α-factor signal sequence.

A polypeptide of the invention may be labelled with a revealing label. The revealing label may be any suitable label which allows the polypeptide to be detected. Suitable labels include radioisotopes, e.g. ^{125}I, ^{35}S enzymes, antibodies, polynucleotides and ligands such as biotin. Labelled polypeptides of the invention may be used in diagnostic procedures such as immunoassays in order to determine the amount of a polypeptide of the invention in a sample. Polypeptides or labelled polypeptides of the invention may also be used in serological or cell mediated immune assays for the detection of immune reactivity to said polypeptides in animals and humans using standard protocols.

A polypeptide or labelled polypeptide of the invention or fragment thereof may also be fixed to a solid phase, for example the surface of an immunoassay well, microparticle, dipstick or biosensor. Such labelled and/or immobilized polypeptides may be

packaged into kits in a suitable container along with suitable reagents, controls, instructions and the like.

Such polypeptides and kits may be used in methods of detection of antibodies or cell mediated immunoreactivity, to the mycobacterial proteins and peptides encoded by the ORFs of the invention and their allelic variants and fragments, using immunoassay. Such host antibodies or cell mediated immune reactivity will occur in humans or animals with an immune system which detects and reacts against polypeptides of the invention. The antibodies may be present in a biological sample from such humans or animals, where the biological sample may be a sample as defined above particularly blood, milk or saliva.

Immunoassay methods are well known in the art and will generally comprise:

(a) providing a polypeptide of the invention comprising an epitope bindable by an antibody against said mycobacterial polypeptide;

(b) incubating a biological sample with said polypeptide under conditions which allow for the formation of an antibody-antigen complex; and

(c) determining whether antibody-antigen complex comprising said polypeptide is formed.

Immunoassay methods for cell mediated immune reactivity in animals and humans are also well known in the art (e.g. as described by Weir et al 1994, J.Immunol Methods 176; 93-101) and will generally comprise

(a) providing a polypeptide of the invention comprising an epitope bindable by a lymphocyte or macrophage or other cell receptor;

(b) incubating a cell sample with said polypeptide under conditions which allow for a cellular immune response such as release of cytokines or other mediator to occur; and

(c) detecting the presence of said cytokine or mediator in the incubate.

Polypeptides of the invention may be made by standard synthetic means well known in the art or recombinantly, as described below.

Polypeptides of the invention or fragments thereof labelled or unlabelled may also be used to identify and characterise different strains of *Mptb*, *Mavs*, other GS-containing pathogenic mycobacteria, or *Mtb*, and properties such as drug resistance or susceptibility.

The polypeptides of the invention may conveniently be packaged in the form of a test kit in a suitable container. In such kits the polypeptide may be bound to a solid support where the assay format for which the kit is designed requires such binding. The kit may also contain suitable reagents for treating the sample to be examined, control reagents, instructions, and the like.

The use of polypeptides of the invention in the diagnosis of inflammatory diseases such as Crohn's disease or sarcoidosis in humans or Johne's disease in animals form a preferred aspect of the invention. The polypeptides may also be used in the prognosis of these diseases. For example, the response of a human or animal subject in response to antibiotic or other therapies may be monitored by utilizing the diagnostic methods of the invention over the course of a period of treatment and following such treatment.

The use of *Mtb* polypeptides of the invention in the above-described methods form a further aspect of the invention, particularly for the detection, diagnosis or prognosis of *Mtb* infections.

Polypeptides of the invention may also be used in assay methods for identifying candidate chemical compounds which will be useful in inhibiting, binding to or disrupting the function of said polypeptides required for pathogenicity. In general, such assays involve bringing the polypeptide into contact with a candidate inhibitor compound and observing the ability of the compound to disrupt, bind to or interfer with the polypeptide.

There are a number of ways in which the assay may be formatted. For example, those polypeptides which have an enzymatic function may be assayed using labelled substrates for the enzyme, and the amount of, or rate of, conversion of the substrate into a product measured, e.g by chromatograpy such as HPLC or by a colourimetric assay. Suitable labels include ^{35}S, ^{125}I, biotin or enzymes such as horse radish peroxidase.

For example, the gene product of ORF C is believed to have GDP-mannose dehydratase activty. Thus an assay for inhbitors of the gene product may utilise for example labelled GDP-mannose, GDP or mannose and the activity of the gene product followed. ORF D encodes a gene related to the synthesis and regulation of capuslar polysaccharides, which are often associated with invasiveness and pathogenicity. Labelled polysaccharide substrates may be used in assays of the ORF D gene product. The gene product of ORF F encodes a protein with putative glucosyl transferase activity and thus labelled amino sugars such as β-1-3-N-acetylglucosamine may be used as substrates in assays.

Candidate chemical compounds which may be used may be natural or synthetic chemical compounds used in drug screening programmes. Extracts of plants which contain several characterised or uncharacterised components may also be used.

Alternatively, the a polypeptide of the invention may be screened against a panel of peptides, nucleic acids or other chemical functionalities which are generated by combinatorial chemistry. This will allow the definition of chemical entities which bind to polypeptides of the invention. Typically, the polypeptide of the invention will be brought into contact with a panel of compounds from a combinantorial library, with either the panel or the polypeptide being immobilized on a solid phase, under conditions suitable for the polypeptide to bind to the panel. The solid phase will then be washed under conditions in which only specific interactions between the polypeptide and individual members of the panel are retained, and those specific members may be utilized in further assays or used to design further panels of candidate ompounds.

For example, a number of assay methods to define peptide interaction with peptides are known. For example, WO86/00991 describes a method for determining mimotopes which comprises making panels of catamer preparations, for example octamers of amino acids, at which one or more of the positions is defined and the remaining positions are randomly made up of other amino acids, determining which catamer binds to a protein of interest and re-screening the protein of interest against a further panel based on the most reactive catamer in which one or more additional designated positions are systematically varied. This may be repeated throughout a number of cycles and used to build up a sequence of a binding candidate compound of interest.

WO89/03430 describes screening methods which permit the preparation of specific mimotopes which mimic the immunological activity of a desired analyte. These mimotopes are identified by reacting a panel of individual peptides wherein said peptides are of systematically varying hydrophobicity, amphipathic characteristics and charge patterns, using an antibody against an antigen of interest. Thus in the present case antibodies against the a polypeptide of the inventoin may be employed and mimotope peptides from such panels may be identified.

C. Vectors.

Polynucleotides of the invention can be incorporated into a recombinant replicable vector. The vector may be used to replicate the nucleic acid in a compatible host cell. Thus in a further embodiment, the invention provides a method of making polynucleotides of the invention by introducing a polynucleotide of the invention into a replicable vector, introducing the vector into a compatible host cell, and growing the host cell under conditions which bring about replication of the vector. The vector may be recovered from the host cell. Suitable host cells are described below in connection with expression vectors.

D. Expression Vectors.

Preferably, a polynucleotide of the invention in a vector is operably linked to a control sequence which is capable of providing for the expression of the coding sequence by the host cell, i.e. the vector is an expression vector. The term "operably linked" refers to a juxtaposition wherein the components described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. Such vectors may be transformed into a suitable host cell as described above to provide for expression of a polypeptide of the invention. Thus, in a further aspect the invention provides a process for preparing polypeptides according to the invention which comprises cultivating a host cell transformed or transfected with an expression vector as described above, under conditions to provide for expression by the vector of a coding sequence encoding the polypeptides, and recovering the expressed polypeptides.

A further embodiment of the invention provides vectors for the replication and expression of polynucleotides of the invention, or fragments thereof. The vectors may be for example, plasmid, virus or phage vectors provided with an origin of replication, optionally a promoter for the expression of the said polynucleotide and optionally a regulator of the promoter. The vectors may contain one or more selectable marker genes, for example an ampicillin resistance gene in the case of a bacterial plasmid or a neomycin resistance gene for a mammalian vector. Vectors may be used *in vitro*, for example for the production of RNA or used to transfect or transform a host cell. The vector may also be adapted to be used *in vivo*, for example in a method of naked DNA vaccination or gene therapy. A further embodiment of the invention provides host cells transformed or transfected with the vectors for the replication and expression of polynucleotides of the invention, including the DNA of GS, the open reading frames thereof and other corresponding ORFs particularly ORFs B, C, E and F from *Mtb*. The cells will be chosen to be compatible with the said vector and may for example be bacterial, yeast, insect or mammalian.

Expression vectors are widely available in the art and can be obtained commercially. Mammalian expression vectors may comprise a mammalian or viral promoter. Mammalian promoters include the metallothionien promoter. Viral promoters include promoters from adenovirus, the SV40 large T promoter and retroviral LTR promoters. Promoters compatible with insect cells include the polyhedrin promoter. Yeast promoters include the alcohol dehydrogenase promoter. Bacterial promoters include the β-galactosidase promoter.

The expression vectors may also comprise enhancers, and in the case of eukaryotic vectors polyadenylation signal sequence downstream of the coding sequence being expressed.

Polypeptides of the invention may be expressed in suitable host cells, for example bacterial, yeast, plant, insect and mammalian cells, and recovered using standard purification techniques including, for example affinity chromatography, HPLC or other chromatographic separation techniques.

Polynucleotides according to the invention may also be inserted into the vectors described above in an antisense orientation in order to provide for the production of antisense RNA. Antisense RNA or other antisense polynucleotides or ligands may also be produced by synthetic means. Such antisense polynucleotides may be used in a method of controlling the levels of the proteins encoded by the ORFs of the invention in a mycobacterial cell.

Polynucleotides of the invention may also be carried by vectors suitable for gene therapy methods. Such gene therapy methods include those designed to provide vaccination against diseases caused by pathogenic mycobacteria or to boost the immune response of a human or animal infected with a pathogenic mycobacteria.

For example, Ziegner *et al*, AIDS, 1995, 9;43-50 describes the use of a replication defective recombinant amphotropic retrovirus to boost the immune response in patients with HIV infection. Such a retrovirus may be modified to carry a polynucleotide encoding a polypeptide or fragment thereof of the invention and the

retrovirus delivered to the cells of a human or animal subject in order to provide an immune response against said polypeptide. The retrovirus may be delivered directly to the patient or may be used to infecte cells *ex-vivo*, e.g. fibroblast cells, which are then introduced into the patient, optionally after being inactivated. The cells are desirably autologous or HLA-matched cells from the human or animal subject.

Gene therapy methods including methods for boosting an immune response to a particluar pathogen are disclosed generally in for example WO95/14091, the disclosure of which is incoporated herein by reference. Recombinant viral vectors include retroviral vectors, adenoviral vectors, adeno-associated viral vectors, vaccinia virus vectors, herpes virus vectors and alphavirus vectors. Alpha virus vectors are described in, for example, WO95/07994, the disclosure of which is incorporated herein by reference.

Where direct administration of the recombinant viral vector is contemplated, either in the form of naked nucleic acid or in the form of packaged particles carrying the nucleic acid this may be done by any suitable means, for example oral administration or intravenous injection. From 10^5 to 10^8 c.f.u of virus represents a typical dose, which may be repeated for example weekly over a period of a few months. Administration of autologous or HLA-matched cells infected with the virus may be more convenient in some cases. This will generally be achieved by administering doses, for example from 10^5 to 10^8 cells per dose which may be repeated as described above.

The recombinant viral vector may further comprise nucleic acid capable of expressing an accessory molecule of the immune system designed to increase the immune response. Such a moleclue may be for example and interferon, particularly interferon gamma, an interleukin, for example IL-1α, IL-1β or IL-2, or an HLA class I or II moleclue. This may be particularly desirable where the vector is intended for use in the treatment of humans or animals already infected with a mycobacteria and it is desired to boost the immune response.

E. Antibodies.

The invention also provides monoclonal or polyclonal antibodies to polypeptides of the invention or fragments thereof. The invention further provides a process for the production of monoclonal or polyclonal antibodies to polypeptides of the invention. Monoclonal antibodies may be prepared by conventional hybridoma technology using the polypeptides of the invention or peptide fragments thereof, as immunogens. Polyclonal antibodies may also be prepared by conventional means which comprise inoculating a host animal, for example a rat or a rabbit, with a polypeptide of the invention or peptide fragment thereof and recovering immune serum.

In order that such antibodies may be made, the invention also provides polypeptides of the invention or fragments thereof haptenised to another polypeptide for use as immunogens in animals or humans.

For the purposes of this invention, the term "antibody", unless specified to the contrary, includes fragments of whole antibodies which retain their binding activity for a polypeptide of the invention. Such fragments include Fv, F(ab') and $F(ab')_2$ fragments, as well as single chain antibodies. Furthermore, the antibodies and fragments thereof may be humanised antibodies, e.g. as described in EP-A-239400.

Antibodies may be used in methods of detecting polypeptides of the invention present in biological samples (where such samples include the human or animal body samples, and environmental samples, mentioned above) by a method which comprises:

(a) providing an antibody of the invention;

(b) incubating a biological sample with said antibody under conditions which allow for the formation of an antibody-antigen complex; and

(c) determining whether antibody-antigen complex comprising said antibody is formed.

Antibodies of the invention may be bound to a solid support for example an immunoassay well, microparticle, dipstick or biosensor and/or packaged into kits in a suitable container along with suitable reagents, controls, instructions and the like.

Antibodies of the invention may be used in the detection, diagnosis and prognosis of diseases as described above in relation to polypeptides of the invention.

F. Compositions.

The present invention also provides compositions comprising a polynucleotide or polypeptide of the invention together with a carrier or diluent. Compositions of the invention also include compositions comprising a nucleic acid, particularly and expression vector, of the invention. Compositions further include those carrying a recombinant virus of the invention. Such compositions include pharmaceutical compositions in which case the carrier or diluent will be pharmaceutically acceptable.

Pharmaceutically acceptable carriers or diluents include those used in formulations suitable for inhalation as well as oral, parenteral (e.g. intramuscular or intravenous or transcutaneous) administration. The formulations may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. Such methods include the step of bringing into association the active ingredient with the carrier which constitutes one or more accessory ingredients. In general the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product.

For example, formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions which may contain anti-oxidants, buffers, bacteriostats and solutes which render the formulation isotonic with the blood of the intended recipient, and aqueous and non-aqueous sterile suspensions which may include suspending agents and thickening

agents, and liposomes or other microparticulate systems which are designed to target the polynucleotide or the polypeptide of the invention to blood components or one or more organs, or to target cells such as M cells of the intestine after oral administration.

G. Vaccines.

In another aspect, the invention provides novel vaccines for the prevention and treatment of infections caused by *Mptb, Mavs*, other GS-containing pathogenic mycobacteria and *Mtb* in animals and humans. The term "vaccine" as used herein means an agent used to stimulate the immune system of a vertebrate, particularly a warm blooded vertebrate including humans, so as to provide protection against future harm by an organism to which the vaccine is directed or to assist in the eradication of an organism in the treatment of established infection. The immune system will be stimulated by the production of cellular immunity antibodies, desirably neutralizing antibodies, directed to epitopes found on or in a pathogenic mycobacterium which expresses any one of the ORFs of the invention. The antibody so produced may be any of the immunological classes, such as the immunoglobulins A, D, E, G or M. Vaccines which stimulate the production of IgA are interest since this is the principle immunoglobulin produced by the secretory system of warm-blooded animals, and the production of such antibodies will help prevent infection or colonization of the intestinal tract. However an IgM and IgG response will also be desirable for systemic infections such as Crohn's disease or tuberculosis.

Vaccines of the invention include polynucleotides of the invention or fragments thereof in suitable vectors and administered by injection of naked DNA using standard protocols. Polynucleotides of the invention or fragments thereof in suitable vectors for the expression of the polypeptides of the invention may be given by injection, inhalation or by mouth. Suitable vectors include *M.bovis* BCG, *M.smegmatis* or other mycobacteria, *Corynebacteria, Salmonella* or other agents according to established protocols.

Polypeptides of the invention or fragments thereof in substantially isolated form may be used as vaccines by injection, inhalation, oral administration or by transcutaneous application according to standard protocols. Adjuvants (such as Iscoms or polylactide-coglycolide encapsulation), cytokines such as IL-12 and other immunomodulators may be used for the selective enhancement of the cell mediated or humoral immunological responses. Vaccination with polynucleotides and/or polypeptides of the invention may be undertaken to increase the susceptibility of pathogenic mycobacteria to antimicrobial agents *in vivo*.

In instances wherein the polypeptide is correctly configured so as to provide the correct epitope, but is too small to be immunogenic, the polypeptide may be linked to a suitable carrier.

A number of techniques for obtaining such linkage are known in the art, including the formation of disulfide linkages using N-succinimidyl-3-(2-pyridylthio) propionate (SPDP) and succinimidyl 4-(N-maleimido-methyl)cyclohexane-1-carboxylate (SMCC) obtained from Pierce Company, Rockford, Illinois, (if the peptide lacks a sulfhydryl group, this can be provided by addition of a cysteine residue). These reagents create a disulfide linkage between themselves and peptide cysteine residues on one protein and an amide linkage through the epsilon-amino on a lysine, or other free amino group in the other. A variety of such disulfide/amide-forming agents are known. See, for example, Immun Rev (1982) 62:185. Other bifunctional coupling agents form a thioether rather than a disulfide linkage. Many of these thio-ether-forming agents are commercially available and include reactive esters of 6-maleimidocaproic acid, 2-bromoacetic acid, 2-iodoacetic acid, 4-(N-maleimido-methyl)cyclohexane-1-carboxylic acid, and the like. The carboxyl group can be activated by combining them with succinimide or 1-hydroxyl-2-nitro-4-sulfonic acid, sodium salt. Additional methods of coupling antigens employs the rotavirus/"binding peptide" system described in EPO Pub. No. 259,149, the disclosure of which is incorporated herein by reference. The foregoing list is not meant to be exhaustive, and modifications of the named compounds can clearly be used.

Any carrier may be used which does not itself induce the production of antibodies harmful to the host. Suitable carriers are typically large, slowly metabolized macromolecules such as proteins; polysaccharides, such as latex functionalized Sepharose®, agarose, cellulose, cellulose beads and the like; polymeric amino acids, such as polyglutamic acid, polylysine, polylactide-coglycolide and the like; amino acid copolymers; and inactive virus particles. Especially useful protein substrates are serum albumins, keyhole limpet hemocyanin, immunoglobulin molecules, thyroglobulin, ovalbumin, tetanus toxoid, and other proteins well known to those skilled in the art.

The immunogenicity of the epitopes may also be enhanced by preparing them in mammalian or yeast systems fused with or assembled with particle-forming proteins such as, for example, that associated with hepatitis B surface antigen. See, e.g., US-A-4,722,840. Constructs wherein the epitope is linked directly to the particle-forming protein coding sequences produce hybrids which are immunogenic with respect to the epitope. In addition, all of the vectors prepared include epitopes specific to HBV, having various degrees of immunogenicity, such as, for example, the pre-S peptide.

In addition, portions of the particle-forming protein coding sequence may be replaced with codons encoding an epitope of the invention. In this replacement, regions which are not required to mediate the aggregation of the units to form immunogenic particles in yeast or mammals can be deleted, thus eliminating additional HBV antigenic sites from competition with the epitope of the invention.

Vaccines may be prepared from one or more immunogenic polypeptides of the invention. These polypeptides may be expressed in various host cells (e.g., bacteria, yeast, insect, or mammalian cells), or alternatively may be isolated from viral preparations or made synthetically.

In addition to the above, it is also possible to prepare live vaccines of attenuated microorganisms which express one or more

recombinant polypeptides of the invention. Suitable attenuated microorganisms are known in the art and include, for example, viruses (e.g., vaccinia virus), as well as bacteria.

The preparation of vaccines which contain an immunogenic polypeptide(s) as active ingredients, is known to one skilled in the art. Typically, such vaccines are prepared as injectables, or as suitably encapsulated oral preparations and either liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injestion or injection may also be prepared. The preparation may also be emulsified, or the protein encapsulated in liposomes. The active immunogenic ingredients are often mixed with excipients which are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants which enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminum hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine (CGP 19835A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2% squalene/Tween® 80 emulsion. The effectiveness of an adjuvant may be determined by measuring the amount of antibodies directed against an immunogenic polypeptide containing an antigenic sequence resulting from administration of this polypeptide in vaccines which are also comprised of the various adjuvants.

The vaccines are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories, oral formulations or as

enemas. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1% - 2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10% - 95% of active ingredient, preferably 25% - 70%.

The proteins may be formulated into the vaccine as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

The vaccines are administered in a manner compatible with the dosage formulation, and in such amount as will be prophylactically and/or therapeutically effective. The quantity to be administered, which is generally in the range of 5μg to 250μg, of antigen per dose, depends on the subject to be treated, capacity of the subject's immune system to synthesize antibodies, mode of administration and the degree of protection desired. Precise amounts of active ingredient required to be administered may depend on the judgement of the practitioner and may be peculiar to each subject.

The vaccine may be given in a single dose schedule, or preferably in a multiple dose schedule. A multiple dose schedule is one in which a primary course of vaccination may be with 1-10 separate doses, followed by other doses given at subsequent time intervals

required to maintain and or reenforce the immune response, for example, at 1-4 months for a second dose, and if needed, a subsequent dose(s) after several months. The dosage regimen will also, at least in part, be determined by the need of the individual and be dependent upon the judgement of the practitioner.

In a further aspect of the invention, there is provided an attenuated vaccine comprising a normally pathogenic mycobacteria which harbours an attenuating mutation in any one of the genes encoding a polypeptide of the invention. The gene is selected from the group of ORFs A, B, C, D, E, F, G and H, including the homologous ORFs B, C, E and F in *Mtb*.

The mycobacteria may be used in the form of killed bacteria or as a live attenuated vaccine. There are advantages to a live attenuated vaccine. The whole live organism is used, rather than dead cells or selected cell components which may exhibit modified or denatured antigens. Protein antigens in the outer membrane will maintain their tertiary and quaternary structures. Therefore the potential to elicit a good protective long term immunity should be higher.

The term "mutation" and the like refers to a genetic lesion in a gene which renders the gene non-functional. This may be at either the level of transcription or translation. The term thus envisages deletion of the entire gene or substantial portions thereof, and also point mutations in the coding sequence which result in truncated gene products unable to carry out the normal function of the gene.

A mutation introduced into a bacterium of the invention will generally be a non-reverting attenuating mutation. Non-reverting means that for practical purposes the probability of the mutated gene being restored to its normal function is small, for example less than 1 in 10^6 such as less than 1 in 10^9 or even less than 1 in 10^{12}.

An attenuated mycobacteria of the invention may be in isolated form. This is usually desirable when the bacterium is to be used for the purposes of vaccination. The term "isolated" means that the bacterium is in a form in which it can be cultured, processed or otherwise used in a form in which it can be readily identified and in which it is substantially uncontaminated by other bacterial strains, for example non-attenuated parent strains or unrelated bacterial strains. The term "isolated bacterium" thus encompasses cultures of a bacterial mutant of the invention, for example in the form of colonies on a solid medium or in the form of a liquid culture, as well as frozen or dried preparations of the strains.

In a preferred aspect, the attenuated mycobacterium further comprises at least one additional mutation. This may be a mutation in a gene responsible for the production of products essential to bacterial growth which are absent in a human or animal host. For example, mutations to the gene for aspartate semi-aldehyde dehydrogenase (*asd*) have been proposed for the production of attenuated strains of Salmonella. The *asd* gene is described further in Gene (1993) 129; 123-128. A lesion in the *asd* gene, encoding the enzyme aspartate β-semialdehyde dehydrogenase would render the organism auxotrophic for the essential nutrient diaminopelic acid (DAP), which can be provided exogenously during bulk culture of the vaccine strain. Since this compound is an essential constituent of the cell wall for gram-negative and some gram-positive organisms and is absent from mammalian or other vertebrate tissues, mutants would undergo lysis after about three rounds of division in such tissues. Analogous mutations may be made to the attenuated mycobacteria of the invention.

In addition or in the alternative, the attenuated mycobacteria may carry a *recA* mutation. The *recA* mutation knocks out homologous recombination - the process which is exploited for the construction of the mutations. Once the *recA* mutation has been incorporated the strain will be unable to repair the constructed deletion mutations. Such a mutation will provide attenuated strains in which the possibility of homologous recombination to

with DNA from wild-type strains has been minimized. *Rec*A genes have been widely studied in the art and their sequences are available. Further modifications may be made for additional safety.

The invention further provides a process for preparing a vaccine composition comprising an attenuated bacterium according to the invention process comprises (a) inoculating a culture vessel containing a nutrient medium suitable for growth of said bacterium; (b) culturing said bacterium; (c) recovering said bacteria and (d) mixing said bacteria with a pharmaceutically acceptable diluent or carrier.

Attenuated bacterial strains according to the invention may be constructed using recombinant DNA methodology which is known per se. In general, bacterial genes may be mutated by a process of targeted homologous recombination in which a DNA construct containing a mutated form of the gene is introduced into a host bacterium which it is desired to attenuate. The construct will recombine with the wild-type gene carried by the host and thus the mutated gene may be incorporated into the host genome to provide a bacterium of the present invention which may then be isolated.

The mutated gene may be obtained by introducing deletions into the gene, e.g by digesting with a restriction enzyme which cuts the coding sequence twice to excise a portion of the gene and then religating under conditions in which the excised portion is not reintroduced into the cut gene. Alternatively frame shift mutations may be introduced by cutting with a restriction enzyme which leaves overhanging 5' and 3' termini, filling in and/or trimming back the overhangs, and religating. Similar mutations may be made by site directed mutagenesis. These are only examples of the types of techniques which will readily be at the disposal of those of skill in the art.

Various assays are available to detect successful recombination. In the case of attenuations which mutate a target gene necessary for the production of an essential metabolite or catabolite

compound, selection may be carried out by screening for bacteria unable to grow in the absence of such a compound. Bacteria may also be screened with antibodies or nucleic acids of the invention to determine the absence of production of a mutated gene product of the invention or to confirm that the genetic lesion introduced - e.g. a deletion - has been incorporated into the genome of the attenuated strain.

The concentration of the attenuated strain in the vaccine will be formulated to allow convenient unit dosage forms to be prepared. Concentrations of from about 10^4 to 10^9 bacteria per ml will generally be suitable, e.g. from about 10^5 to 10^8 such as about 10^6 per ml. Live attenuated organisms may be administered subcutaneously or intramuscularly at up to 10^8 organisms in one or more doses, e.g from around 10^5 to 10^8, e.g about 10^6 or 10^7 organisms in a single dose.

The vaccines of the invention may be administered to recipients to treat established disease or in order to protect them against diseases caused by the corresponding wild type mycobacteria, such as inflammatory diseases such as Crohn's disease or sarcoidosis in humans or Johne's disease in animals. The vaccine may be administered by any suitable route. In general, subcutaneous or intramuscular injection is most convenient, but oral, intranasal and colorectal administration may also be used.

The following Examples illustrates aspects of the invention.

EXAMPLE 1

Tests for the presence of the GS identifier sequence were performed on 5µl bacterial DNA extracts (25 µg/ml to 500 µg/ml) using polymerase chain reaction based on the oligonucleotide primers 5'-GATGCCGTGAGGAGGTAAAGCTGC-3' (Seq ID No. 40) and 5'-GATACGGCTCTTGAATCCTGCACG-3' (Seq ID No. 41) from within the identifier DNA sequences (Seq.ID Nos 1 and 2). PCR was performed for 40 cycles in the presence of 1.5 mM magnesium and an annealing temperature of 58°C. The presence or absence of the correct amplification product indicated the presence or absence

of GS identifier sequence in the corresponding bacterium. GS identifier sequence is shown to be present in all the laboratory and field strains of *Mptb* and *Mavs* tested. This includes *Mptb* isolates 0025 (bovine CVL Weybridge), 0021 (caprine, Moredun), 0022 (bovine, Moredun), 0139 (human, Chiodini 1984), 0209, 0208, 0211, 0210, 0212, 0207, 0204, 0206 (bovine, Whipple 1990). All *Mptb* strains were IS*900* positive. The *Mavs* strains include 0010 and 0012 (woodpigeon, Thorel) 0018 (armadillo, Portaels) and 0034, 0037, 0038, 0040 (AIDS, Hoffner). All *Mavs* strains were IS*902* positive. One pathogenic *M.avium* strain 0033 (AIDS, Hoffner) also contained GS identifier sequence. GS identifier sequence is absent from other mycobacteria including other *M.avium, M.malmoense, M.szulgai, M.gordonae, M.chelonei, M.fortuitum, M.phlei,* as well as *E.coli, S.areus, Nocardia* sp, *Streptococcus* sp. *Shigella* sp. *Pseudomonas* sp.

Example 2:

To obtain the full sequence of GS in *Mavs* and *Mptb* we generated a genomic library of *Mavs* using the restriction endonuclease EcoRI and cloning into the vector pUC18. This achieved a representative library which was screened with ^{32}P-labelled identifier sequence yielding a positive clone containing a 17kbp insert. We constructed a restriction map of this insert and identified GS as fragments unique to *Mavs* and *Mptb* and not occurring in laboratory strains of *M.avium*. These fragments were sub-cloned into pUC18 and pGEM4Z. We identified GS contained within an 8kb region. The full nucleotide sequence was determined for GS on both DNA strands using primer walking and automated DNA sequencing. DNA sequence for GS in *Mptb* was obtained using overlapping PCR products generated using PwoDNA polymerase, a proofreading thermostable enzyme. The final DNA sequences were derived using the University of Wisconsin GCG gel assembly software package.

Example 3:

The DNA sequence of GS in *Mavs* and *Mptb* was found to be more than 99% homologous. The ORFs encoded in GS were identified using GeneRunner and DNAStar computer programmes. Eight ORFs were identified and designated GSA, GSB, GSC, GSD, GSE, GSF, GSG

and GSH. Database comparisons were carried out against the GenEMBL Database release version 48.0 (9/96), using the BLAST and BLIXEM programmes. GSA and GSB encoded proteins of 13.5kDa and 30.7kDa respectively, both of unknown functions. GSC encoded a protein of 38.4kDa with a 65% homology to the amino acid sequence of *rfbD* of *V.cholerae*, a 62% amino acid sequence homology to *gmd* of *E.coli* and a 58% homology to *gca* of *Ps.aeruginosa* which are all GDP-D-mannose dehydratases. Equivalent gene products in *H.influenzae*, *S.dysenteriae*, *Y.enterocolitica*, *N.gonorrhoea*, *K.pneumoniae* and *rfbD* in *Salmonella enterica* are all involved in 'O'-antigen processing known to be linked to pathogenicity. GSD encoded a protein of 37.1kDa which showed 58% homology at the DNA level to *wcaG* from *E.coli*, a gene involved in the synthesis and regulation of capsular polysaccharides, also related to pathogenicity. GSE was found to have a > 30% amino acid homology to *rfbT* of *V.cholerae*, involved in the transport of specific LPS components across the cell membrane. In *V.cholerae* the gene product causes a seroconversion from the Inaba to the Ogawa 'epidemic' strain. GSF encoded a protein of 30.2kDa which was homologous in the range 25-40% at the amino acid level to several glucosyl transferases such as *rfpA* of *K.pneumoniae*, *rfbB* of *K.pneumoniae*, *lgtD* of *H.influenzae*, *lsi* of *N.gonorrhoae*. In *E.coli* an equivalent gene *galE* adds β-1-3 N-acetylglucosamine to galactose, the latter only found in 'O' and 'M' antigens which are also related to pathogenicity. GSH comprising the ORFs GSH_1 and GSH_2 encodes a protein totalling about 60kDa which is a putative transposase with a 40 - 43% homology at the amino acid level to the equivalent gene product of *IS21* in *E.coli*. This family of insertion sequences is broadly distributed amongst gram negative bacteria and is responsible for mobility and transposition of genetic elements. An *IS21*- like element in *B.fragilis* is split either side of the β-lactamase gene controlling its activation and expression. We programmed an *E.coli* S30 cell-free extract with plasmid DNA containing the ORF GSH under the control of a *lac* promoter in the presence of a ^{35}S-methionine, and demonstrated the translation of an abundant 60kDa protein.

The proteins homologous to GS encoded in other organisms are in general highly antigenic. Thus the proteins encoded by the ORFs

in GS may be used in immunoassays of antibody or cell mediated immuno-reactivity for diagnosing infections caused by mycobacteria, particularly *Mptb, Mavs and Mtb*. Enhancement of host immune recognition of GS encoded proteins by vaccination using naked specific DNA or recombinant GS proteins, may be used in the prevention and treatment of infections caused by *Mptb, Mavs* and *Mtb* in humans and animals. Mutation or deletion of all or some of the ORFs A to H in GS may be used to generate attenuated strains of *Mptb, Mavs* or *Mtb* with lower pathogenicity for use as living or killed vaccines in humans and animals. Such vaccines are particularly relevant to Johne's disease in animals, to diseases caused by *Mptb* in humans such as Crohn's disease, and to the management of tuberculosis especially where the disease is caused by multiple drug-resistant organisms.

SEQUENCE LISTING

Seq. ID No.1

```
5'- 1 GATCCAACTA AACCCGATGG AACCCCGCGC AAACTATTGG ACGTCTCCGC GCTACGCAGT
   61 TGGGTTGGCG CCCGCGAATC GCACTGAAAG AGGGCATCGA TGCAACGGTG TCGTGGTACC
  121 GCACAAATGC CGATGCCGTG AGGAGGTAAA GCTGCGGGCC GGCCGATGTT ATCCCTCCGG
  181 CCGGACGGGT AGGGCGACCT GCCATCGAGT GGTACGGCAG TCGCCTGGCC GGCGAGGCGC
  241 ATGGCCTATG TGAGTATCCC ATAGCCTGGC TTGGCTCGCC CCTACGCATT ATCAGTTGAC
  301 CGCTTTCGCG CCACGTCGCA GGCTTGCGGC AGCATCCCGT TCAGGTCTCC TCATGGTCCG
  361 GTGTGGCACG ACCACGCAAG CTCGAACCGA CTCGTTTCCC AATTTCGCAT GCTAATATCG
  421 CTCGATGGAT TTTTTGCGCA ACGCCGGCTT GATGGCTCGT AACGTTAGCA CCGAGATGCT
  481 GCGCCACTCC GAACGAAAGC GCCTATTAGT AAACCAAGTC GAAGCATACG GAGTCAACGT
  541 TGTTATTGAT GTCGGTGCTA ACTCCGGCCA GTTCGGTAGC GCTTTGCGTC GTGCAGGATT
  601 CAAGAGCCGT ATCGTTTCCT TTGAACCTCT TTCGGGGCCA TTTGCGCAAC TAACGCGCAA
  661 GTCGGCATCG GATC -3'
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Seq. ID No.2

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5'- 1 GATCCGATGC CGACTTGCGC GTTAGTTGCG CAAATGGCCC CGAAAGAGGT TCAAAGGAAA
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  121 CGACATCAAT AACAACGTTG ACTCCGTATG CTTCGACTTG GTTTACTAAT AGGCGCTTTC
  181 GTTCGGAGTG GCGCAGCATC TCGGTGCTAA CGTTACGAGC CATCAAGCCG GCGTTGCGCA
  241 AAAAATCCAT CGAGCGATAT TAGCATGCGA AATTGGGAAA CGAGTCGGTT CGAGCTTGCG
  301 TGGTCGTGCC ACACCGGACC ATGAGGAGAC CTGAACGGGA TGCTGCCGCA AGCCTGCGAC
  361 GTGGCGCGAA AGCGGTCAAC TGATAATGCG TAGGGGCGAG CCAAGCCAGG CTATGGGATA
  421 CTCACATAGG CCATGCGCCT CGCCGGCCAG GCGACTGCCG TACCACTCGA TGGCAGGTCG
  481 CCCTACCCGT CCGGCCGGAG GGATAACATC GGCCGGCCCG CAGCTTTACC TCCTCACGGC
  541 ATCGGCATTT GTGCGGTACC ACGACACCGT TGCATCGATG CCCTCTTTCA GTGCGATTCG
  601 CGGGCGCCAA CCCAACTGCG TAGCGCGGAG ACGTCCAATA GTTTGCGCGG GGTTCCATCG
  661 GGTTTAGTTG GATC -3'
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Seq. ID No.3

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 101  ACGATCACCT TGTACCGGTC GATGTATGAC CCAATGTCGT CCGCAACCGA
 151  GAAGACGTAC GTCAGGTCCG CCGCCCCGCT TTCACCCATG GGCGTCGGGA
 201  CGGCGATGAA AATGACGTCC GCGTGCTCGA TTCCGCGTTG CCGGTCGGTG
 251  GTGAAGTCAA TCAGCCCGTT CTCACGGTTC CTCGCAATCA ACTCCCAACC
 301  CGGGCTCGAA AATCGGGACA CTGCCTGCGA GGAGCAAATC GATCTTGGCC
 351  TGATCGATAT CGACACAGAC GACATCGTTG CCGCTATCCG CGAGACAGGC
 401  GCCCGTGACG AGGCCTACAT AGCCTGATCC GACCACCGAA ATTTTCAAGA
 451  TGACCCCTTC AAGTCCCCGA TCGGTCGACG ACCATACTGC CGCAACTCTG
 501  TACCCTCCGT GGGTAATTCG CATGTCGCGT TCGTAAGGAG CAGCCAGCGA
 551  GTCGGGGACG TTCGGTGAGA GAGTCGCAGG ACTACGAGGT TGCCGGTGCG
 601  ATACATCACA GTGTTGCGTC TGTCGGCAAC GATGCAGCAA GAACCCACGG
 651  GGCAGCCCTG AACTGCGCGC ATGACCGGTC CTTGTCCTGG CACCTTTGAT
 701  CGGCCACCGC TTCCATGCGA ACATGACCGG AATCCATAGC GCGTGGTCAA
 751  GCAGCGGGGA GGTAGACGTC GGTGTCATCT GCTCCAACCG TGTCGGTGAT
 801  AACGATTTCG CTGAACGATC TCGAGGGATT GAAAAGCACC GTGGAGAGCG
 851  TTCGCGCGCA GCGCTATGGG GGGCGAATCG AGCACATCGT CATCGACGGT
 901  GGATCGGGCG ACGCCGTCGT GGAGTATCTG TCCGGCGATC CTGGCTTTGC
 951  ATATTGGCAA TCTCAGCCCG ACAACGGGAG ATATGACGCG ATGAATCAGG
1001  GCATTGCCCA TTCGTCGGGC GACCTGTTGT GGTTTATGCA CTCCACGGAT
1051  CGTTTCTCCG ATCCAGATGC AGTCGCTTCC GTGGTGGAGG CGCTCTCGGG
1101  GCATGGACCA GTACGTGATT TGTGGGGTTA CGGGAAAAAC AACCTTGTCG
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1201  AAGATGCGGA AATTTCTGCT CGGCGCGACG GTTGCGCATC AGGCGACATT
1251  CTTCGGCGCG TCGCTGGTAG CCAAGTTGGG CGGTTACGAT CTTGATTTTG
1301  GACTCGAGGC GGACCAGCTG TTCATCTACC GTGCCGCACT AATACGGCCT
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1901  GGGCTCGTTC GTCGAGCTTC GACGTTTAAC ACGTCGCGGA TCGATCACCT
1951  CTACGTTGAC CCACACCAAC CGGGCGCGCG CTTGTTCTTG CACTATGCAG
2001  ACCTCACTGA CGGCACCCGG TTGGTGACCC TGCTCAGCAG TATCGACCCG
2051  GATGAGGTCT ACAACCTCGC AGCGCAGTCC CATGTGCGCG TCAGCTTTGA
2101  CGAGCCAGTG CATACCGGAG ACACCACCGG CATGGGATCG ATCCGACTTC
2151  TGGAAGCAGT CCGCCTTTCT CGGGTGGACT GCCGGTTCTA TCAGGCTTCC
2201  TCGTCGGAGA TGTTCGGCGC ATCTCCGCCA CCGCAGAACG AATCGACGCC
2251  GTTCTATCCC CGTTCGCCAT ACGGCGCGGC CAAGGTCTTC TCGTACTGGA
2301  CGACTCGCAA CTATCGAGAG GCGTACGGAT TATTCGCAGT GAATGGCATC
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2501  GTCGAGGGGA TGTGGAGGAT GTTGCAAGCG CCTGAACCTG ATGACTACGT
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2751  GCATCATGGT GGACGCGGAC ATCGCCGCGT TGGAGTGCGA TGGCACACCA
2801  TGGATCGACA CGCCGATGTT GCCTGGTTGG GGCAGAGTAA GTTGACGACT
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3051  GGCCGCACGG GTCGGCGGCA TCATGGCGAA TAACACCTAT CCCGCGGACT
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3151  GCCGTGCGTG TGCCGCGGCT CCTTTTCCTC GGTTCGTCAT GCATCTACCC
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3251  TGGAGCCCAC CAACGACGCG TATGCGATCG CCAAGATCGC CGGTATCCTG
3301  CAAGTTCAGG CGGTTAGGCG CCAATATGGG CTGGCGTGGA TCTCTGCGAT
3351  GCCGACTAAC CTCTACGGAC CCGGCGACAA CTTCTCCCCG TCCGGGTCGC
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4001  TCTCCTCATG GTCCGGTGTG GCACGACCAC GCAAGCTCGA ACCGACTCGT
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4251  GGATTCAAGA GCCGTATCGT TTCCTTTGAA CCTCTTTCGG GGCCATTTGC
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4351  ATGCCCTAGG CGACGCCGAT GAGACGATTA CCATCAATGT GGCAGGCAAT
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4501  TTGATTCGGT TGCATCAGAA TTTCTGAACC CTACCGATGT TACTTTCCTG
4551  AAGATCGACG TACAGGGTTT CGAGAAGCAG GTTATCACGG GCAGTAAGTC
4601  AACGCTTAAC GAAAGCTGCG TCGGCATGCA ACTCGAACTT TCTTTTATTC
4651  CGTTGTACGA AGGTGACATG CTGATTCATG AAGCGCTTGA ACTTGTCTAT
4701  TCCCTAGGTT TCAGACTGAC GGGTTTGTTG CCCGGCTTTA CGGATCCGCG
4751  CAATGGTCGA ATGCTTCAAG CTGACGGCAT TTTCTTCCGT GGGGACGATT
4801  GACATAAATG CTCCGTCGGC ACCCTGCCGG TATCCAAACG GGCGATCTGG
4851  TGAGCCGGCC TCCCGGGCAC CTAATCGACT ATCTAAATTG AGGCGGCCGC
4901  GACGTGCGGC ACGAACAGGT GGCCGGCTGC TAGCGTTACA CACGTCATGA
4951  CTGCGCCAGT GTTCTCGATA ATTATCCCTA CCTTCAATGC AGCGGTGACG
5001  CTGCAAGCCT GCCTCGGAAG CATCGTCGGG CAGACCTACC GGGAAGTGGA
5051  AGTGGTCCTT GTCGACGGCG GTTCGACCGA TCGGACCCTC GACATCGCGA
5101  ACAGTTTCCG CCCGGAACTC GGCTCGCGAC TGGTCGTTCA CAGCGGGCCC
5151  GATGATGGCC CCTACGACGC CATGAACCGC GGCGTCGGCG TGGCCACAGG
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5251  CGTTGGCCCA GGTAGCCGCT TTTCTCGGCG ACCATGCGGC AAGCCATCTT
5301  GTCTATGGCG ATGTTGTGAT GCGTTCGACG AAAAGCCGGC ATGCCGGACC
5351  TTTCGACCTC GACCGCCTCC TATTTGAGAC GAATTTGTGC CACCAATCGA
5401  TCTTTTACCG CCGTGAGCTT TTCGACGGCA TCGGCCCTTA CAACCTGCGC
5451  TACCGAGTCT GGGCGGACTG GGACTTCAAT ATTCGCTGCT TCTCCAACCC
5501  GGCGCTGATT ACCCGCTACA TGGACGTCGT GATTTCCGAA TACAACGACA
5551  TGACCGGCTT CAGCATGAGG CAGGGGACTG ATAAAGAGTT CAGAAAACGG
5601  CTGCCAATGT ACTTCTGGGT TGCAGGGTGG GAGACTTGCA GGCGCATGCT
5651  GGCGTTTTTG AAAGACAAGG AGAATCGCCG TCTGGCCTTG CGTACGCGGT
5701  TGATAAGGGT TAAGGCCGTC TCCAAAGAAC GAAGCGCAGA ACCGTAGTCG
5751  CGGATCCACA TTGGACTTCT TTAACGCGTT TGCGTCCTGA TCCACCTTTC
5801  AAGCCCGTTC CGCGTAACGC GGCGCGCAGA GAGTGGTCGC ATATCGCATC
5851  ACTGTTCTCG TGCCAGTGCT TGGAAAGCGT CGAGCACTCT GGTTCGCGTT
5901  CTTGACGTTC GCGCCCGCTC CTAGAGGTAG CGTGTCACGT GACTGAAGCC
5951  AATGAGTGCA ACTCGGCGTC GCGAAAGGTT TCAGTCGCGG TTGAGCAAGA
6001  CACCGCAAGA CTACTGGAGT GCGTGCACAA GCGCCTCCAG CTCGCGGCTG
6051  AAAGCGGATG CAAAGGGATT CGAAGCTTGA GCAACATGCG AAGGGGAGAA
6101  CGGCCTATGA GGCTGGGACA GGTTTTCGAT CCGCGCGCGA ATGCACTGTC
6151  AATGGCCAAG TAGAAGTCCC CGCTGGTGGC CAGCAGAAGT CCCCACTCCG
6201  CTGCGGGTGG TTGGCTAATT CTTGGCGGCT CCCTTCTTGT GGTCGGCGTG
6251  GCGCATCCGG TAGGACTCGC CGGAGGTGAC GACGATGCTG GCGTGGTGCA
6301  GCAGCCGATC GAGGATGCTG GCGGCGGTGG TGTGCTCGGG CAGGAATCGC
6351  CCCCATTGTT CGAAGGGCCA ATGCGAGGCG ATGGCCAGGG AGCGGCGCTC
6401  GTAGCCGGCA GCCACGAGCC GGAACAACAG TTGAGTCCCG GTGTCGTCGA
6451  GCGGGGCGAA GCCGATCTCG TCCAAGATGA CCAGATCCGC GCGGAGCAGG
6501  GTGTCGATGA TCTTGCCGAC GGTGTTGTCG GCCAGGCCGC GGTAGAGGAC
6551  CTCGATCAGG TCGGCGGCGG TGAAGTAGCG GACTTTGAAT CCGGCGTGGA
6601  CGGCAGCGTG CCCGCAGCCG ATGAGCAGGT GACTTTTGCC CGTACCAGGT
6651  GGGCCAATGA CCGCCAGGTT CTGTTGTGCC CGAATCCATT CCAGGCTCGA
6701  CAGGTAGTCG AACGTGGCTG CGGTGATCGA CGATCCGGTG ACGTCGAACC
6751  CGTCGAGGGT CTTGGTGACC GGGAAGGCTG CGGCCTTGAG ACGGTTGGCG
6801  GTGTTGGAGG CATCGCGGGC AGCGATCTCG GCCTCAACCA ACGTCCGCAG
6851  GATCTCCTCC GGTGTCCAGC GTTGCGTCTT GGCGACTTGC AACACCTCGG
6901  CGGCGTTGCG GCGCACCGTG GCCAGCTTCA ACCGCCGCAG CGCCGCGTCA
6951  AGGTCAGCAG CCAGCGGTGC CGCCGAGGAC GGTGCCACCG GCTTGGCAGC
7001  GGTGGTCATG AGGCCGTCCC GTCGGTGGTG TTGATCTTGT AGGCCTCCAA
7051  CGAGCGGGTC TCGACGGTGG GCAGATCGAG CACGAGTGCG TCGCCGGCGG
7101  GGCGGGGTTG TGGGGTGCCG GCGCCGGCGG CCAGGATCGA GCGCACGTCG
7151  GCAGCGCGGA ACCGGCGAAA CGCAACCGCC CGGCGCAGCG CGTCAATCAA
7201  AGCCTGTTCG CCGTGGGCGG CGCCAAGGCC GAGCAGAATG TCGAGTTCGG
7251  ATTTCAGTCG GGTGTTGCCG ATCGCAGCAG CACCGACGAG GAACTGCTGC
7301  GCTTCGGTTC CCAATGCGCA GAATCGTTTC TCTGCTTGGG TTTTCGGGCG
7351  AGGACCACGC GAGGGTGCGG GTCTGGGTCC GTCGTAGTGT TCATCGAGGA
7401  TGGACACCTC ACCTGGGCTG ACGAGCTCGT GCTCGGCCAC GATCACACCG
7451  GTCGCAGGTT CCAACAGGAT CAGGGCGCCA TGATCGACCA CCACCGCCAC
7501  GGTGGCACCG ACGAGCCGCT GAGGCACCGA GTAACGAGCT GAGCCGTAAC
7551  GGATGCACGA GAGGCCGTCG ACCTTACGGC GCACCGACCC CGAGCCGATC
7601  GTCGGCCGCA GCGAGGGCAG CTCCCTCAAG ACGGTGCGCT CGTCAACCAA
7651  GCGATCGTTG GGCACGGCGC AGATCTCCGA GTGGACCGTG GCATTGACCT
7701  CGGCGCACCA TAGTTGCGCC TGGGCGTTGA GGGCACGTAG GTCGACCTGC
7751  TCACCGGCTA ACGCAGCTTC GGTCAGCAGC GGCACCGCAA GGTCGTCCTG
7801  AGCGTAGCCA CAGAGGTTCT CCACGATGCC CTTCGATTGC GGATCCGCAC
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7851  CGTGGCAGAA GTCCGGAACG AAGCCATAGT GGGACGCGAA TCGCACATAA
7901  TCCGGTGTTG GAACAACAAC ATTGGCGACG ACACCACCTT TGAGGCAGCC
7951  CATCCGGTCG GCCAGGATCT TGGCCGGAAC CCCACCGATC GCCTC
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Seq. ID No.4

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   1 TTCTACTGCC TGACCTGAGC AGCGCCGAGG CGCGCAGCGC GATCACTGCG ACCTGAATGG
  61 CCAGGTGGAA AGCGCCACCG ATCCCGGCAC CGAGTGCCTG ACGATTCGGA TCCCTTGCAC
 121 CACAACGAGA GTGAGACCGC CATGATGACG AAATATCGGC TGGGCGGAGT CAACGCCGGA
 181 GTGACAAAAG TGAGAACCCG GTGAAGCGAG CGCTTATAAC AGGGATCACG GGGCAGGATG
 241 GTTCCTACCT CGCCGAGCTA CTACTGAGCA AGGGATACGA GGTTCACGGG CTCGTTCGTC
 301 GAGCTTCGAC GTTTAACACG TCGCGGATCG ATCACCTCTA CGTTGACCCA CACCAACCGG
 361 GCGCGCGCTT GTTCTTGCAC TATGCAGACC TCACTGACGG CACCCGGTTG GTGACCCTGC
 421 TCAGCAGTAT CGACCCGGAT GAGGTCTACA ACCTCGCAGC GCAGTCCCAT GTGCGCGTCA
 481 GCTTTGACGA GCCAGTGCAT ACCGGAGACA CCACCGGCAT GGGATCGATC CGACTTCTGG
 541 AAGCAGTCCG CCTTTCTCGG GTGGACTGCC GGTTCTATCA GGCTTCCTCG TCGGAGATGT
 601 TCGGCGCATC TCCGCCACCG CAGAACGAAT CGACGCCGTT CTATCCCCGT TCGCCATACG
 661 GCGCGGCCAA GGTCTTCTCG TACTGGACGA CTCGCAACTA TCGAGAGGCG TACGGATTAT
 721 TCGCAGTGAA TGGCATCTTG TTCAACCATG AGTCCCCCCG GCGCGGCGAG ACTTTCGTGA
 781 CCCGAAAGAT CACGCGTGCC GTGGCGCGCA TCCGAGCTGG CGTCCAATCG GAGGTCTATA
 841 TGGGCAACCT CGATGCGATC CGCGACTGGG GCTACGCGCC CGAATATGTC GAGGGGATGT
 901 GGAGGATGTT GCAAGCGCCT GAACCTGATG ACTACGTCCT GGCGACAGGG CGTGGTTACA
 961 CCGTACGTGA GTTCGCTCAA GCTGCTTTTG ACCACGTCGG GCTCGACTGG CAAAAGCACG
1021 TCAAGTTTGA CGACCGCTAT TTGCGCCCCA CCGAGGTCGA TTCGCTAGTA GGAGATGCCG
1081 ACAGGGCGGC CCAGTCACTC GGCTGGAAAG CTTCGGTTCA TACTGGTGAA CTCGCGCGCA
1141 TCATGGTGGA CGCGGACATC GCCGCGTCGG AGTGCGATGG CACACCATGG ATCGACACGC
1201 CGATGTTGCC TGGTTGGGGC GGAGTAAGTT GACGACTACA CCTGGGCCTC TGGACCGCGC
1261 AACGCCCGTG TATATCGCCG GTCATCGGGG GCTGGTCGGC TCAGCGCTCG TACGTAGATT
1321 TGAGGCCGAG GGGTTCACCA ATCTCATTGT GCGATCACGC GATGAGATTG ATCTGACGGA
1381 CCGAGCCGCA ACGTTTGATT TTGTGTCTGA GACAAGACCA CAGGTGATCA TCGATGCGGC
1441 CGCACGGGTC GGCGGCATCA TGGCGAATAA CACCTATCCC GCGGACTTCT TGTCCGAAAA
1501 CCTCCGAATC CAGACCAATT TGCTCGACGC AGCTGTCGCC GTGCGTGTGC CGCGGCTCCT
1561 TTTCCTCGGT TCGTCATGCA TCTACCCGAA GTACGCTCCG CAACCTATCC ACGAGAGTGC
1621 TTTATTGACT GGCCCTTTGG AGCCCACCAA CGACGCGTAT GCGATCGCCA AGATCGCCGG
1681 TATCCTGCAA GTTCAGGCGG TTAGGCGCCA ATATGGGCTG GCGTGGATCT CTGCGATGCC
1741 GACTAACCTC TACGGACCCG GCGACAACTT CTCCCCGTCC GGGTCGCATC TCTTGCCGGC
1801 GCTCATCCGT CGATATGAGG AAGCCAAAGC TGGTGGTGCA GAAGAGGTGA CGAATTGGGG
1861 GACCGGTACT CCGCGGCGCG AACTTCTGCA TGTCGACGAT CTGGCGAGCG CATGCCTGTT
1921 CCTTTTGGAA CATTTCGATG GTCCGAACCA CGTCAACGTG GGCACCGGCG TCGATCACAG
1981 CATTAGCGAG ATCGCAGACA TGGTCGCTAC GGCGGTGGGC TACATCGGCG AAACACGTTG
2041 GGATCCAACT AAACCCGATG GAACCCCGCG CAAACTATTG GACGTCTCCG CGCTACGCGA
2101 GTTGGGTTGG CGCCCGCGAA TCGCACTGAA AGACGGCATC GATGCAACGG TGTCGTGGTA
2161 CCGCACAAAT GCCGATGCCG TGAGGAGGTA AAGCTGCGGG CCGGCCGATG TTATCCCTCC
2221 GGCCGGACGG GTAGGGCGAC CTGCCATCGA GTGGTACGGC AGTCGCCTGG CCGGCGAGGC
2281 GCATGGCCTA TGGGAGTATC CCATAGCCTG GCTTGGCTCG CCCCTACGCA TTATCAGTTG
2341 ACCGCTTTCG CGCCAGCTCG CAGGCTCGCG GCAGCATCCC GTTCAGGTCT CCTCATGGTC
2401 CGGTGTGGCA CGACCACGCA AGCTCGAACC GACTCGTTTC CCAATTTCGC ATGCTAATAT
2461 CGCTCGATGG ATTTTTTGCG CAACGCCGGC TTGATGGCTC GTAACGTTAG CACCGAGATG
2521 CTGCGCCACT TCGAACGAAA GCGCCTATTA GTAAACCAAT TCAAAGCATA CGGAGTCAAC
2581 GTTGTTATTG ATGTCGGTGC TAACTCCGGC CAGTTCGGTA GCGCTTTGCG TCGTGCAGGA
2641 TTCAAGAGCC GTATCGTTTC CTTTGAACCT CTTTCGGGGC CATTTGCGCA ACTAACGCGC
2701 GAGTCGGCAT CGGATCCACT ATGGGAGTGT CACCAGTATG CCCTAGGCGA CGCCGATGAG
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2761 ACGATTACCA TCAATGTGGC AGGCAATGCG GGGGCAAGTA GTTCCGTGCT GCCGATGCTT
2821 AAAAGTCATC AAGATGCCTT TCCTCCCGCG AATTATATTG GCACCGAAGA CGTTGCAATA
2881 CACCGCCTTG ATTCGGTTGC ATCAGAATTT CTGAACCCTA CCGATGTTAC TTTCCTGAAG
2941 ATCGACGTAC AGGGTTTCGA GAAGCAGGTT ATCGCGGGCA GTAAGTCAAC GCTTAACGAA
3001 AGCTGCGTCG GCATGCAACT CGAACTTTCT TTTATTCCGT TGTACGAAGG TGACATGCTG
3061 ATTCATGAAG CGCTTGAACT TGTCTATTCC CTAGGTTTCA GACTGACGGG TTTGTTGCCC
3121 GGATTTACGG ATCCGCGCAA TGGTCGAATG CTTCAAGCTG ACGGCATTTT CTTCCGTGGG
3181 GACGATTGAC ATAAATGCTT GCGTCGGCAC CCTGCCGGTA TCCAAACGGG CGATCTGGTG
3241 AGCCGGCCTC CCGGGCACCT AATCGACTAT CTAAATTGAG GCGGCCGCGA CGTGCGGCAC
3301 GAACAGGTGG CCGGCTGCTA GCGTTACACA CGTCATGACT GCGCCAGTGT TCTCGATAAT
3361 TATCCCTACC TTCAATGCAG CGGTGACGCT GCAAGCCTGC CTCGGAAGCA TCGTCGGGCA
3421 GACCTACCGG GAAGTGGAAG TGGTCCTTGT CGACGGCGGT TCGACCGATC GGACCCTCGA
3481 CATCGCGAAC AGTTTCCGCC CGGAACTCGG CTCGCGACTG GTCGTTCACA GCGGGCCCGA
3541 TGATGGCCCC TACGACGCCA TGAACCGCGG CGTCGGCGTA GCCACAGGCG AATGGGTACT
3601 TTTTTTAGGC GCCGACGACA CCCTCTACGA ACCAACCACG TTGGCCCAGG TAGCCGCTTT
3661 TCTCGGCGAC CATGCGGCAA GCCATCTTGT CTATGGCGAT GTTGTGATGC GTTCGACGAA
3721 AAGCCGGCAT GCCGGACCTT TCGACCTCGA CCGCCTCCTA TTTGAGACGA ATTTGTGCCA
3781 CCAATCGATC TTTTACCGCC GTGAGCTTTT CGACGGCATC GGCCCTTACA ACCTGCGCTA
3841 CCGAGTCTGG GCGGACTGGG ACTTCAATAT TCGCTGCTTC TCCAACCCGG CGCTGATTAC
3901 CCGCTACATG GACGTCGTGA TTTCCGAATA CAACGACATG ACCGGCTTCA GCATGAGGCA
3961 GGGGACTGAT AAAGAGTTCA GAAAACGGCT GCCAATGTAC TTCTGGGTTG CAGGGTGGGA
4021 GACTTGCAGG CGCATGCTGG CGTTTTTGAA AGACAAGGAG AATCGCCGTC TGGCCTTGCG
4081 TACGCGGTTG ATAAGGGTTA AGGCCGTCTC CAAAGAACGA AGCGCAGAAC CGTAGTCGCG
4141 GATCCACATT GGACTTCTTT AACGCGTTTG CGTCCTGATC CACCTTTCAA CCCCGTTCCG
4201 CGTGACGCGG CGCGCAGAGA GTGGTCGCAT ATCGCGTCAC TGTTCTCGTG CCAGTGCTTG
4261 GAAAGCGTCG AGCACTCTGG TTCGCGTTCT TGACGTTCGC GCCCGCCCCT AGAGGTAGCG
4321 TGTCACGTGA CTGAAGCCAA TGAGTGCAAC TCGGCGTCGC GAAAGGTTTC AGTCGCGGTT
4381 GAGCAAGACA CCGCAAGACT ACTGGAGTGC GTGCACAAGC GCCTCCAGCT CACGG
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Seq. ID No.5

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  61 ttgtaccggt cgatgtatga cccaatgtcg tccgcaaccg agaagacgta cgtcaggtcc
 121 gccgccccgc tttcacccat gggcgtcggg acggcgatga aaatgacgtc cgcgtgctcg
 181 attccgcgtt gccggtcggt ggtgaagtca atcagcccgt tctcacggtt cctcgcaatc
 241 aactcccaac ccgggctcga aaatcgggac actgcctgcg aggagcaaat cgatcttggc
 301 ctgatcgata tcgacacaga cgacatcgtt gccgctatcc gcgagacagg cgcccgtgac
 361 gaggcctaca tagcctga
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Seq. ID No.6

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 31 S A T E K T Y V R S A A P L S P M G V G T A M K M T S A C S
 61 I P R C R S V V K S I S P F S R F L A I N S Q P G L E N R D
 91 T A C E E Q I D L G L I D I D T D D I V A A I R E T G A R D
121 E A Y I A
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Seq. ID No.7

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   1 gtgtcatctg ctccaaccgt gtcggtgata acgatttcgc tgaacgatct cgagggattg
  61 aaaagcaccg tggagagcgt tcgcgcgcag cgctatgggg ggcgaatcga gcacatcgtc
 121 atcgacggtg gatcgggcga cgccgtcgtg gagtatctgt ccggcgatcc tggctttgca
 181 tattggcaat ctcagcccga caacgggaga tatgacgcga tgaatcaggg cattgcccat
 241 tcgtcgggcg acctgttgtg gtttatgcac tccacggatc gtttctccga tccagatgca
 301 gtcgcttccg tggtggaggc gctctcgggg catggaccag tacgtgattt gtggggttac
 361 gggaaaaaca accttgtcgg actcgacggc aaaccacttt tccctcggcc gtacggctat
 421 atgccgttta agatgcggaa atttctgctc ggcgcgacgg ttgcgcatca ggcgacattc
 481 ttcggcgcgt cgctggtagc caagttgggc ggttacgatc ttgattttgg actcgaggcg
 541 gaccagctgt tcatctaccg tgccgcacta atacggcctc ccgtcacgat cgaccgcgtg
 601 gtttgcgact tcgatgtcac gggacctggt tcaacccagc ccatccgtga gcactatcgg
 661 accctgcggc ggctctggga cctgcatggc gactacccgc tgggtgggcg cagagtgtcg
 721 tgggcttact tgcgtgtgaa ggagtacttg attcgggccg acctggccgc attcaacgcg
 781 gtaaagttct tgcgagcgaa gttcgccaga gcttcgcgga agcaaaattc atag
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Seq. ID No.8

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   1  V S S A P T V S V I T I S L N D L E G L K S T V E S V R A Q
  31  R Y G G R I E H I V I D G G S G D A V V E Y L S G D P G F A
  61  Y W Q S Q P D N G R Y D A M N Q G I A H S S G D L L W F M H
  91  S T D R F S D P D A V A S V V E A L S G H G P V R D L W G Y
 121  G K N N L V G L D G K P L F P R P Y G Y M P F K M R K F L L
 151  G A T V A H Q A T F F G A S L V A K L G G Y D L D F G L E A
 181  D Q L F I Y R A A L I R P P V T I D R V V C D F D V T G P G
 211  S T Q P I R E H Y R T L R R L W D L H G D Y P L G G R R V S
 241  W A Y L R V K E Y L I R A D L A A F N A V K F L R A K F A R
 271  A S R K Q N S
```

Seq. ID No.9

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   1 gtgaagcgag cgcttataac agggatcacg gggcaggatg gttcctacct cgccgagcta
  61 ctactgagca agggatacga ggttcacggg ctcgttcgtc gagcttcgac gtttaacacg
 121 tcgcggatcg atcacctcta cgttgaccca caccaaccgg gcgcgcgctt gttcttgcac
 181 tatgcagacc tcactgacgg cacccggttg gtgaccctgc tcagcagtat cgacccggat
 241 gaggtctaca acctcgcagc gcagtcccat gtgcgcgtca gctttgacga gccagtgcat
 301 accggagaca ccaccggcat gggatcgatc cgacttctgg aagcagtccg cctttctcgg
 361 gtggactgcc ggttctatca ggcttcctcg tcggagatgt tcggcgcatc tccgccaccg
 421 cagaacgaat cgacgccgtt ctatccccgt tcgccatacg gcgcggccaa ggtcttctcg
 481 tactggacga ctcgcaacta tcgagaggcg tacggattat tcgcagtgaa tggcatcttg
 541 ttcaaccatg agtccccccg gcgcggcgag actttcgtga cccgaaagat cacgcgtgcc
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 901 ggctggaaag cttcggttca tactggtgaa ctcgcgcgca tcatggtgga cgcggacatc
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1021 agagtaagtt ga
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Seq. ID No.10

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  31  L V R R A S T F N T S R I D H L Y V D P H Q P G A R L F L H
  61  Y A D L T D G T R L V T L L S S I D P D E V Y N L A A Q S H
  91  V R V S F D E P V H T G D T T G M G S I R L L E A V R L S R
 121  V D C R F Y Q A S S S E M F G A S P P P Q N E S T P F Y P R
 151  S P Y G A A K V F S Y W T T R N Y R E A Y G L F A V N G I L
 181  F N H E S P R R G E T F V T R K I T R A V A R I R A G V Q S
 211  E V Y M G N L D A I R D W G Y A P E Y V E G M W R M L Q A P
 241  E P D D Y V L A T G R G Y T V R E F A Q A A F D H V G L D W
 271  Q K R V K F D D R Y L R P T E V D S L V G D A D K A A Q S L
 301  G W K A S V H T G E L A R I M V D A D I A A L E C D G T P W
 331  I D T P M L P G W G R V S
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Seq. ID No.11

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 121 tcgcggatcg atcacctcta cgttgaccca caccaaccgg gcgcgcgctt gttcttgcac
 181 tatgcagacc tcactgacgg cacccggttg gtgaccctgc tcagcagtat cgacccggat
 241 gaggtctaca acctcgcagc gcagtcccat gtgcgcgtca gctttgacga gccagtgcat
 301 accggagaca ccaccggcat gggatcgatc cgacttctgg aagcagtccg cctttctcgg
 361 gtggactgcc ggttctatca ggcttcctcg tcggagatgt tcggcgcatc tccgccaccg
 421 cagaacgaat cgacgccgtt ctatccccgt tcgccatacg gcgcggccaa ggtcttctcg
 481 tactggacga ctcgcaacta tcgagaggcg tacggattat tcgcagtgaa tggcatcttg
 541 ttcaaccatg agtccccccg gcgcggcgag actttcgtga cccgaaagat cacgcgtgcc
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 841 ttgcgcccca ccgaggtcga ttcgctagta ggagatgccg acagggcggc ccagtcactc
 901 ggctggaaag cttcggttca tactggtgaa ctcgcgcgca tcatggtgga cgcggacatc
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1021 ggagtaagtt ga
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Seq. ID No.12

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   1  V K R A L I T G I T G Q D G S Y L A E L L L S K G Y E V H G
  31  L V R R A S T F N T S R I D H L Y V D P H Q P G A R L F L H
  61  Y A D L T D G T R L V T L L S S I D P D E V Y N L A A Q S H
  91  V R V S F D E P V H T G D T T G M G S I R L L E A V R L S R
 121  V D C R F Y Q A S S S E M F G A S P P P Q N E S T P F Y P R
 151  S P Y G A A K V F S Y W T T R N Y R E A Y G L F A V N G I L
 181  F N H E S P R R G E T F V T R K I T R A V A R I R A G V Q S
 211  E V Y M G N L D A I R D W G Y A P E Y V E G M W R M L Q A P
 241  E P D D Y V L A T G R G Y T V R E F A Q A A F D H V G L D W
 271  Q K H V K F D D R Y L R P T E V D S L V G D A D R A A Q S L
 301  G W K A S V H T G E L A R I M V D A D I A A S E C D G T P W
 331  I D T P M L P G W G G V S
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Seq. ID No.13

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 121 ctggtcggct cagcgctcgt acgtagattt gaggccgagg ggttcaccaa tctcattgtg
 181 cgatcacgcg atgagattga tctgacggac cgagccgcaa cgtttgattt tgtgtctgag
 241 acaagaccac aggtgatcat cgatgcggcc gcacgggtcg gcggcatcat ggcgaataac
 301 acctatcccg cggacttctt gtccgaaaac ctccgaatcc agaccaattt gctcgacgca
 361 gctgtcgccg tgcgtgtgcc gcggctcctt ttcctcggtt cgtcatgcat ctacccgaag
 421 tacgctccgc aacctatcca cgagagtgct ttattgactg gccctttgga gcccaccaac
 481 gacgcgtatg cgatcgccaa gatcgccggt atcctgcaag ttcaggcggt taggcgccaa
 541 tatgggctgg cgtggatctc tgcgatgccg actaaccttt acggacccgg cgacaacttc
 601 tccccgtccg ggtcgcatct cttgccggcg ctcatccgtc gatatgagga agccaaagct
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 721 gtcgacgatc tggcgagcgc atgcctgttc cttttggaac atttcgatgg tccgaaccac
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 841 gcggtgggct acatcggcga aacacgttgg gatccaacta aacccgatgg aaccccgcgc
 901 aaactattgg acgtctccgc gctacgcgag ttgggttggc gcccgcgaat cgcactgaaa
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Seq. ID No.14

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   1  V R W H T M D R H A D V A W L G Q S K L T T T P G P L D R A
  31  T P V Y I A G H R G L V G S A L V R R F E A E G F T N L I V
  61  R S R D E I D L T D R A A T F D F V S E T R P Q V I I D A A
  91  A R V G G I M A N N T Y P A D F L S E N L R I Q T N L L D A
 121  A V A V R V P R L L F L G S S C I Y P K Y A P Q P I H E S A
 151  L L T G P L E P T N D A Y A I A K I A G I L Q V Q A V R R Q
 181  Y G L A W I S A M P T N L Y G P G D N F S P S G S H L L P A
 211  L I R R Y E E A K A G G A E E V T N W G T G T P R R E L L H
 241  V D D L A S A C L F L L E H F D G P N H V N V G T G V D H S
 271  I S E I A D M V A T A V G Y I G E T R W D P T K P D G T P R
 301  K L L D V S A L R E L G W R P R I A L K D G I D A T V S W Y
 331  R T N A D A V R R
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Seq. ID No.15

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   1 gtgcgatggc acaccatgga tcgacacgcc gatgttgcct ggttggggcg gagtaagttg
  61 acgactacac ctgggcctct ggaccgcgca acgcccgtgt atatcgccgg tcatcggggg
 121 ctggtcggct cagcgctcgt acgtagattt gaggccgagg ggttcaccaa tctcattgtg
 181 cgatcacgcg atgagattga tctgacggac cgagccgcaa cgtttgattt tgtgtctgag
 241 acaagaccac aggtgatcat cgatgcggcc gcacgggtcg gcggcatcat ggcgaataac
 301 acctatcccg cggacttctt gtccgaaaac ctccgaatcc agaccaattt gctcgacgca
 361 gctgtcgccg tgcgtgtgcc gcggctcctt ttcctcggtt cgtcatgcat ctacccgaag
 421 tacgctccgc aacctatcca cgagagtgct ttattgactg gccctttgga gcccaccaac
 481 gacgcgtatg cgatcgccaa gatcgccggt atcctgcaag ttcaggcggt taggcgccaa
 541 tatgggctgg cgtggatctc tgcgatgccg actaacctct acggacccgg cgacaacttc
 601 tccccgtccg ggtcgcatct cttgccggcg ctcatccgtc gatatgagga agccaaagct
 661 ggtggtgcag aagaggtgac gaattggggg accggtactc cgcggcgcga acttctgcat
 721 gtcgacgatc tggcgagcgc atgcctgttc cttttggaac atttcgatgg tccgaaccac
 781 gtcaacgtgg gcaccggcgt cgatcacagc attagcgaga tcgcagacat ggtcgctacg
 841 gcggtgggct acatcggcga aacacgttgg gatccaacta aacccgatgg aaccccgcgc
 901 aaactattgg acgtctccgc gctacgcgag ttgggttggc gcccgcgaat cgcactgaaa
 961 gacggcatcg atgcaacggt gtcgtggtac cgcacaaatg ccgatgccgt gaggaggtaa
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Seq. ID No.16

```
   1  V R W H T M D R H A D V A W L G R S K L T T T P G P L D R A
  31  T P V Y I A G H R G L V G S A L V R R F E A E G F T N L I V
  61  R S R D E I D L T D R A A T F D F V S E T R P Q V I I D A A
  91  A R V G G I M A N N T Y P A D F L S E N L R I Q T N L L D A
 121  A V A V R V P R L L F L G S S C I Y P K Y A P Q P I H E S A
 151  L L T G P L E P T N D A Y A I A K I A G I L Q V Q A V R R Q
 181  Y G L A W I S A M P T N L Y G P G D N F S P S G S H L L P A
 211  L I R R Y E E A K A G G A E E V T N W G T G T P R R E L L H
 241  V D D L A S A C L F L L E H F D G P N H V N V G T G V D H S
 271  I S E I A D M V A T A V G Y I G E T R W D P T K P D G T P R
 301  K L L D V S A L R E L G W R P R I A L K D G I D A T V S W Y
 331  R T N A D A V R R
```

Seq. ID No.17

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   1 atggattttt tgcgcaacgc cggcttgatg gctcgtaacg ttagtaccga gatgctgcgc
  61 cacttcgaac gaaagcgcct attagtaaac caattcaaag catacggagt caacgttgtt
 121 attgatgtcg gtgctaactc cggccagttc ggtagcgctt tgcgtcgtgc aggattcaag
 181 agccgtatcg tttcctttga acctctttcg gggccatttg cgcaactaac gcgcaagtcg
 241 gcatcggatc cactatggga gtgtcaccag tatgccctag gcgacgccga tgagacgatt
 301 accatcaatg tggcaggcaa tgcgggggca agtagttccg tgctgccgat gcttaaaagt
 361 catcaagatg cctttcctcc cgcgaattat attggcaccg aagacgttgc aatacaccgc
 421 cttgattcgg ttgcatcaga atttctgaac cctaccgatg ttactttcct gaagatcgac
 481 gtacagggtt tcgagaagca ggttatcacg ggcagtaagt caacgcttaa cgaaagctgc
 541 gtcggcatgc aactcgaact ttcttttatt ccgttgtacg aaggtgacat gctgattcat
 601 gaagcgcttg aacttgtcta ttccctaggt ttcagactga cgggtttgtt gcccggcttt
 661 acggatccgc gcaatggtcg aatgcttcaa gctgacggca ttttcttccg tggggacgat
 721 tga
```

Seq. ID No.18

```
  1 M D F L R N A G L M A R N V S T E M L R H F E R K R L L V N
 31 Q F K A Y G V N V V I D V G A N S G Q F G S A L R R A G F K
 61 S R I V S F E P L S G P F A Q L T R K S A S D P L W E C H Q
 91 Y A L G D A D E T I T I N V A G N A G A S S S V L P M L K S
121 H Q D A F P P A N Y I G T E D V A I H R L D S V A S E F L N
151 P T D V T F L K I D V Q G F E K Q V I T G S K S T L N E S C
181 V G M Q L E L S F I P L Y E G D M L I H E A L E L V Y S L G
211 F R L T G L L P G F T D P R N G R M L Q A D G I F F R G D D
```

Seq. ID No.19

```
   1 atggattttt tgcgcaacgc cggcttgatg gctcgtaacg ttagcaccga gatgctgcgc
  61 cacttcgaac gaaagcgcct attagtaaac caattcaaag catacggagt caacgttgtt
 121 attgatgtcg gtgctaactc cggccagttc ggtagcgctt tgcgtcgtgc aggattcaag
 181 agccgtatcg tttcctttga acctctttcg gggccatttg cgcaactaac gcgcgagtcg
 241 gcatcggatc cactatggga gtgtcaccag tatgccctag gcgacgccga tgagacgatt
 301 accatcaatg tggcaggcaa tgcgggggca agtagttccg tgctgccgat gcttaaaagt
 361 catcaagatg cctttcctcc cgcgaattat attggcaccg aagacgttgc aatacaccgc
 421 cttgattcgg ttgcatcaga atttctgaac cctaccgatg ttactttcct gaagatcgac
 481 gtacagggtt tcgagaagca ggttatcgcg ggcagtaagt caacgcttaa cgaaagctgc
 541 gtcggcatgc aactcgaact ttcttttatt ccgttgtacg aaggtgacat gctgattcat
 601 gaagcgcttg aacttgtcta ttccctaggt ttcagactga cgggtttgtt gcccggattt
 661 acggatccgc gcaatggtcg aatgcttcaa gctgacggca ttttcttccg tggggacgat
 721 tga
```

Seq. ID No.20

```
  1 M D F L R N A G L M A R N V S T E M L R H F E R K R L L V N
 31 Q F K A Y G V N V V I D V G A N S G Q F G S A L R R A G F K
 61 S R I V S F E P L S G P F A Q L T R E S A S D P L W E C H Q
 91 Y A L G D A D E T I T I N V A G N A G A S S S V L P M L K S
121 H Q D A F P P A N Y I G T E D V A I H R L D S V A S E F L N
151 P T D V T F L K I D V Q G F E K Q V I A G S K S T L N E S C
181 V G M Q L E L S F I P L Y E G D M L I H E A L E L V Y S L G
211 F R L T G L L P G F T D P R N G R M L Q A D G I F F R G D D
```

Seq. ID No.21

```
   1 atgactgcgc cagtgttctc gataattatc cctaccttca atgcagcggt gacgctgcaa
  61 gcctgcctcg gaagcatcgt cgggcagacc taccgggaag tggaagtggt ccttgtcgac
 121 ggcggttcga ccgatcggac cctcgacatc gcgaacagtt tccgcccgga actcggctcg
 181 cgactggtcg ttcacagcgg gcccgatgat ggcccctacg acgccatgaa ccgcggcgtc
 241 ggcgtggcca caggcgaatg ggtacttttt ttaggcgccg acgacaccct ctacgaacca
 301 accacgttgg cccaggtagc cgcttttctc ggcgaccatg cggcaagcca tcttgtctat
 361 ggcgatgttg tgatgcgttc gacgaaaagc cggcatgccg gacctttcga cctcgaccgc
 421 ctcctatttg agacgaattt gtgccaccaa tcgatctttt accgccgtga gcttttcgac
 481 ggcatcggcc cttacaacct gcgctaccga gtctgggcgg actgggactt caatattcgc
 541 tgcttctcca acccggcgct gattacccgc tacatggacg tcgtgatttc cgaatacaac
 601 gacatgaccg gcttcagcat gaggcagggg actgataaag agttcagaaa acggctgcca
 661 atgtacttct gggttgcagg gtgggagact tgcaggcgca tgctggcgtt tttgaaagac
 721 aaggagaatc gccgtctggc cttgcgtacg cggttgataa gggttaaggc cgtctccaaa
 781 gaacgaagcg cagaaccgta g
```

Seq. ID No.22

```
   1  M T A P V F S I I I P T F N A A V T L Q A C L G S I V G Q T
  31  Y R E V E V V L V D G G S T D R T L D I A N S F R P E L G S
  61  R L V V H S G P D D G P Y D A M N R G V G V A T G E W V L F
  91  L G A D D T L Y E P T T L A Q V A A F L G D H A A S H L V Y
 121  G D V V M R S T K S R H A G P F D L D R L L F E T N L C H Q
 151  S I F Y R R E L F D G I G P Y N L R Y R V W A D W D F N I R
 181  C F S N P A L I T R Y M D V V I S E Y N D M T G F S M R Q G
 211  T D K E F R K R L P M Y F W V A G W E T C R R M L A F L K D
 241  K E N R R L A L R T R L I R V K A V S K E R S A E P
```

Seq. ID No.23

```
   1 atgactgcgc cagtgttctc gataattatc cctaccttca atgcagcggt gacgctgcaa
  61 gcctgcctcg gaagcatcgt cgggcagacc taccgggaag tggaagtggt ccttgtcgac
 121 ggcggttcga ccgatcggac cctcgacatc gcgaacagtt tccgcccgga actcggctcg
 181 cgactggtcg ttcacagcgg gcccgatgat ggcccctacg acgccatgaa ccgcggcgtc
 241 ggcgtagcca caggcgaatg ggtacttttt ttaggcgccg acgacaccct ctacgaacca
 301 accacgttgg cccaggtagc cgcttttctc ggcgaccatg cggcaagcca tcttgtctat
 361 ggcgatgttg tgatgcgttc gacgaaaagc cggcatgccg gacctttcga cctcgaccgc
 421 ctcctatttg agacgaattt gtgccaccaa tcgatctttt accgccgtga gcttttcgac
 481 ggcatcggcc cttacaacct gcgctaccga gtctgggcgg actgggactt caatattcgc
 541 tgcttctcca acccggcgct gattacccgc tacatggacg tcgtgatttc cgaatacaac
 601 gacatgaccg gcttcagcat gaggcagggg actgataaag agttcagaaa acggctgcca
 661 atgtacttct gggttgcagg gtgggagact tgcaggcgca tgctggcgtt tttgaaagac
 721 aaggagaatc gccgtctggc cttgcgtacg cggttgataa gggttaaggc cgtctccaaa
 781 gaacgaagcg cagaaccgta g
```

Seq. ID No.24

```
  1 M T A P V F S I I I P T F N A A V T L Q A C L G S I V G Q T
 31 Y R E V E V V L V D G G S T D R T L D I A N S F R P E L G S
 61 R L V V H S G P D D G P Y D A M N R G V G V A T G E W V L F
 91 L G A D D T L Y E P T T L A Q V A A F L G D H A A S H L V Y
121 G D V V M R S T K S R H A G P F D L D R L L F E T N L C H Q
151 S I F Y R R E L F D G I G P Y N L R Y R V W A D W D F N I R
181 C F S N P A L I T R Y M D V V I S E Y N D M T G F S M R Q G
211 T D K E F R K R L P M Y F W V A G W E T C R R M L A F L K D
241 K E N R R L A L R T R L I R V K A V S K E R S A E P
```

Seq. ID No.25

```
   1 gtggccagca gaagtcccca ctccgctgcg ggtggttggc taattcttgg cggctccctt
  61 cttgtggtcg gcgtggcgca tccggtagga ctcgccggag gtgacgacga tgctggcgtg
 121 gtgcagcagc cgatcgagga tgctggcggc ggtggtgtgc tcgggcagga atcgcccccа
 181 ttgttcgaag ggccaatgcg aggcgatggc cagggagcgg cgctcgtagc cggcagccac
 241 gagccggaac aacagttgag tcccggtgtc gtcgagcggg gcgaagccga tctcgtccaa
 301 gatgaccaga tccgcgcgga gcagggtgtc gatgatcttg ccgacggtgt tgtcggccag
 361 gccgcggtag aggacctcga tcaggtcggc ggcggtgaag tagcggactt tgaatccggc
 421 gtggacggca gcgtgcccgc agccgatgag caggtgactt ttgcccgtac caggtgggcc
 481 aatgaccgcc aggttctgtt gtgcccgaat ccattccagg ctcgacaggt agtcgaacgt
 541 ggctgcggtg atcgacgatc cggtgacgtc gaacccgtcg agggtcttgg tgaccgggaa
 601 ggctgcggcc ttgagacggt tggcggtgtt ggaggcatcg cgggcagcga tctcggcctc
 661 aaccaacgtc cgcaggatct cctccggtgt ccagcgttgc gtcttggcga cttgcaacac
 721 ctcggcggcg ttgcggcgca ccgtggccag cttcaaccgc cgcagcgccg cgtcaaggtc
 781 agcagccagc ggtgccgccg aggacggtgc caccggcttg gcagcggtgg tcatgaggcc
 841 gtcccgtcgg tggtgttgat cttgtag
```

Seq. ID No.26

```
  1 V A S R S P H S A A G G W L I L G G S L L V V G V A H P V G
 31 L A G G D D D A G V V Q Q P I E D A G G G G V L G Q E S P P
 61 L F E G P M R G D G Q G A A L V A G S H E P E Q Q L S P G V
 91 V E R G E A D L V Q D D Q I R A E Q G V D D L A D G V V G Q
121 A A V E D L D Q V G G G E V A D F E S G V D G S V P A A D E
151 Q V T F A R T R W A N D R Q V L L C P N P F Q A R Q V V E R
181 G C G D R R S G D V E P V E G L G D R E G C G L E T V G G V
211 G G I A G S D L G L N Q R P Q D L L R C P A L R L G D L Q H
241 L G G V A A H R G Q L Q P P Q R R V K V S S Q R C R R G R C
271 H R L G S G G H E A V P S V V L I L
```

Seq. ID No.27

```
   1 atgggctgcc tcaaaggtgg tgtcgtcgcc aatgttgttg ttccaacacc ggattatgtg
  61 cgattcgcgt cccactatgg cttcgttccg gacttctgcc acggtgcgga tccgcaatcg
 121 aagggcatcg tggagaacct ctgtggctac gctcaggacg accttgcggt gccgctgctg
 181 accgaagctg cgttagccgg tgagcaggtc gacctacgtg ccctcaacgc ccaggcgcaa
 241 ctatggtgcg ccgaggtcaa tgccacggtc cactcggaga tctgcgccgt gcccaacgat
 301 cgcttggttg acgagcgcac cgtcttgagg gagctgccct cgctgcggcc gacgatcggc
 361 tcggggtcgg tgcgccgtaa ggtcgacggc ctctcgtgca tccgttacgg ctcagctcgt
 421 tactcggtgc ctcagcggct cgtcggtgcc accgtggcgg tggtggtcga tcatggcgcc
 481 ctgatcctgt tggaacctgc gaccggtgtg atcgtggccg agcacgagct cgtcagccca
 541 ggtgaggtgt ccatcctcga tgaacactac gacggaccca gacccgcacc ctcgcgtggt
 601 cctcgcccga aaacccaagc agagaaacga ttctgcgcat tgggaaccga agcgcagcag
 661 ttcctcgtcg gtgctgctgc gatcggcaac acccgactga aatccgaact cgacattctg
 721 ctcggccttg gcgccgccca cggcgaacag gctttgattg acgcgctgcg ccgggcggtt
 781 gcgtttcgcc ggttccgcgc tgccgacgtg cgctcgatcc tggccgccgg cgccggcacc
 841 ccacaacccc gccccgccgg cgacgcactc gtgctcgatc tgcccaccgt cgagacccgc
 901 tcgttggagg cctacaagat caacaccacc gacgggacgg cctcatgacc accgctgcca
 961 agccggtggc accgtcctcg gcggcaccgc tggctgctga ccttgacgcg gcgctgcggc
1021 ggttgaagct ggccacggtg cgccgcaacg ccgccgaggt gttgcaagtc gccaagacgc
1081 aacgctggac accggaggag atcctgcgga cgttggttga ggccgagatc gctgcccgcg
1141 atgcctccaa caccgccaac cgtctcaagg ccgcagcctt cccggtcacc aagaccctcg
1201 acgggttcga cgtcaccgga tcgtcgatca ccgcagccac gttcgactac ctgtcgagcc
1261 tggaatggat tcgggcacaa cagaacctgg cggtcattgg cccacctggt acgggcaaaa
1321 gtcacctgct catcggctgc gggcacgctg ccgtccacgc cggattcaaa gtccgctact
1381 tcaccgccgc cgacctgatc gaggtcctct accgcggcct ggccgacaac accgtcggca
1441 agatcatcga caccctgctc cgcgcggatc tggtcatctt ggacgagatc ggcttcgccc
1501 cgctcgacga caccgggact caactgttgt tccggctcgt ggctgccggc tacgagcgcc
1561 gctccctggc catcgcctcg cattggccct tcgaacaatg ggggcgattc ctgcccgagc
1621 acaccaccgc cgccagcatc ctcgatcggc tgctgcacca cgccagcatc gtcgtcacct
1681 ccggcgagtc ctaccggatg cgccacgccg accacaagaa gggagccgcc aagaattag
```

Seq. ID No.28

```
   1 M G C L K G G V V A N V V V P T P D Y V R F A S H Y G F V P
  31 D F C H G A D P Q S K G I V E N L C G Y A Q D D L A V P L L
  61 T E A A L A G E Q V D L R A L N A Q A Q L W C A E V N A T V
  91 H S E I C A V P N D R L V D E R T V L R E L P S L R P T I G
 121 S G S V R R K V D G L S C I R Y G S A R Y S V P Q R L V G A
 151 T V A V V V D H G A L I L L E P A T G V I V A E H E L V S P
 181 G E V S I L D E H Y D G P R P A P S R G P R P K T Q A E K R
 211 F C A L G T E A Q Q F L V G A A A I G N T R L K S E L D I L
 241 L G L G A A H G E Q A L I D A L R R A V A F R R F R A A D V
 271 R S I L A A G A G T P Q P R P A G D A L V L D L P T V E T R
 301 S L E A Y K I N T T D G T A S
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Seq. ID No.29

```
   1  M T T A A K P V A P S S A A P L A A D L D A A L R R L K L A
  31  T V R R N A A E V L Q V A K T Q R W T P E E I L R T L V E A
  61  E I A A R D A S N T A N R L K A A A F P V T K T L D G F D V
  91  T G S S I T A A T F D Y L S S L E W I R A Q Q N L A V I G P
 121  P G T G K S H L L I G C G H A A V H A G F K V R Y F T A A D
 151  L I E V L Y R G L A D N T V G K I I D T L L R A D L V I L D
 181  E I G F A P L D D T G T Q L L F R L V A A G Y E R R S L A I
 211  A S H W P F E Q W G R F L P E H T T A A S I L D R L L H H A
 241  S I V V T S G E S Y R M R H A D H K K G A A K N
```

Seq. ID No.30

```
   1 gtgacgtctg ctccgaccgt ctcggtgata acgatctcgt tcaacgacct cgacgggttg
  61 cagcgcacgg tgaaaagtgt gcgggcgcaa cgctaccggg gacgcatcga gcacatcgta
 121 atcgacggtg gcagcggcga cgacgtggtg gcatacctgt ccgggtgtga accaggcttc
 181 gcgtattggc agtccgagcc cgacggcggg cggtacgacg cgatgaacca gggcatcgcg
 241 cacgcatcgg gtgatctgtt gtggttcttg cactccgccg atcgtttttc cgggcccgac
 301 gtggtagccc aggccgtgga ggcgctatcc ggcaagggac cggtgtccga attgtggggc
 361 ttcgggatgg atcgtctcgt cgggctcgat cgggtgcgcg gcccgatacc tttcagcctg
 421 cgcaaattcc tggccggcaa gcaggttgtt ccgcatcaag catcgttctt cggatcatcg
 481 ctggtggcca agatcggtgg ctacgacctt gatttcggga tcgccgccga ccaggaattc
 541 atattgcggg ccgcgctggt atgcgagccg gtcacgattc ggtgtgtgct gtgcgagttc
 601 gacaccacgg gcgtcggctc gcaccgggaa ccaagcgcgg tcttcggtga tctgcgccgc
 661 atgggcgacc ttcatcgccg ctacccgttc gggggaaggc gaatatcaca tgcctaccta
 721 cgcggccggg agttctacgc ctacaacagt cgattctggg aaaacgtctt cacgcgaatg
 781 tcgaaatag
```

Seq. ID No.31

```
   1  M T S A P T V S V I T I S F N D L D G L Q R T V K S V R A Q
  31  R Y R G R I E H I V I D G G S G D D V V A Y L S G C E P G F
  61  A Y W Q S E P D G G R Y D A M N Q G I A H A S G D L L W F L
  91  H S A D R F S G P D V V A Q A V E A L S G K G P V S E L W G
 121  F G M D R L V G L D R V R G P I P F S L R K F L A G K Q V V
 151  P H Q A S F F G S S L V A K I G G Y D L D F G I A A D Q E F
 181  I L R A A L V C E P V T I R C V L C E F D T T G V G S H R E
 211  P S A V F G D L R R M G D L H R R Y P F G G R R I S H A Y L
 241  R G R E F Y A Y N S R F W E N V F T R M S K
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Seq. ID No.32

```
   1 gtgaagcgag cgctcatcac cggaatcacc ggccaggacg gctcgtatct cgccgaactg
  61 ctgctggcca aggggtatga ggttcacggg ctcatccggc gcgcttcgac gttcaacacc
 121 tcgcggatcg atcacctcta cgtcgacccg caccaaccgg gcgcgcggct gtttctgcac
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Seq. ID No.35

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Seq. ID No.38

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Seq. ID No.39

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Seq 41:

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CLAIMS

1. A polypeptide in substantially isolated form which comprises a sequence selected from the sequences of Seq.ID.No: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28 and 29, or a polypeptide substantially homologous thereto.

2. A polypeptide in substantially isolated form which comprises a sequence selected from the sequences of Seq.ID.No: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28 and 29.

3. A polypeptide which comprises a fragment of a polypeptide defined in claim 1 or 2, said fragment comprising at least 12 amino acids and an epitope.

4. A polynucleotide in substantially isolated form which encodes a polypeptide according to any one of claims 1 to 3.

5. A polynucleotide in substantially isolated form which is capable of selectively hybridizing to Seq.ID.No: 3 or 4 or a fragment thereof.

6. A polynucleotide fragment according to claim 5 which comprises a sequence selected from the sequences of Seq.ID.No: 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and 27, or a polynucleotide at least 90% homologous thereto.

7. A polynucleotide in substantially isolated form comprising a sequence selected from the sequences of Seq.ID.No: 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and 27.

8. A polynucleotide probe which comprises a fragment of at least 15 nucleotides of a polynucleotide as defined in any one of claims 4 to 7, optionally carrying a revealing label.

9. A recombinant vector carrying a polynucleotide as defined in any one of claims 4 to 7.

10. An antibody capable of binding a polypeptide or fragment thereof as defined in any one of claims 1 to 3.

11. An antibody capable of binding a polypeptide or fragment thereof wherein the polypeptide is a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or is a peptide substantially homogolous thereto.

12. A test kit for detecting the presence or absence of a pathogenic mycobacterium in a sample which comprises a polynucleotide according to any one of claims 4 to 8, a polypeptide according to any one of claims 1 to 3, a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, or an antibody according to, any one of claims 10 or 11.

13. A method of detecting the presence or absence of antibodies in an animal or human, against a pathogenic mycobacteria in a sample which comprises:

(a) providing a polypeptide according to any one of claims 1 to 3 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which comprises an epitope;

(b) incubating a biological sample with said polypeptide under conditions which allow for the formation of an antibody-antigen complex; and

(c) determining whether antibody-antigen complex comprising said polypeptide is formed.

14. A method of detecting the presence or absence of a polypeptide according to any one of claims 1 to 3 or a polypeptide which comprises a sequence selected from the

sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto in a biological sample which method which comprises:

(a) providing an antibody according to any one of claims 10 and 11;

(b) incubating a biological sample with said antibody under conditions which allow for the formation of an antibody-antigen complex; and

(c) determining whether antibody-antigen complex comprising said antibody is formed.

15. A method of detecting the presence or absence of cell mediated immune reactivity in an animal or human, to a polypeptide according to claims 1 to 3 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which method comprises

(a) providing a polypeptide according to any one of claims 1 to 3 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which comprises an epitope;

(b) incubating a cell sample with said polypeptide under conditions which allow for a cellular immune response such as release of cytokines or other mediator or reaction to occur; and

(c) detecting the presence of said cytokine or mediator or cellular response in the incubate.

16. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 3 in a suitable carrier or diluent.

17. A composition according to claim 16 or a composition comprising a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto,

for use in the treatment or prevention of diseases caused by mycobacteria.

18. A method of treating or preventing mycobacterial disease in an animal or human caused by mycobacteria which express a polypeptide according to claims 1 to 3 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which method comprises vaccinating or treating an animal or human with an effective amount of said polypeptide.

19. A method of treating or preventing mycobacterial diseases in animals or humans caused by mycobacteria containing the polynucleotide of Seq.ID.No: 3 or 4, which method comprises vaccinating or treating an animal or human with an effective amount of a polynucleotide according to claims 4 to 7, a vector according to claim 9 or a polynucleotide which encodes a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto.

20. A method according to claims 18 or 19 for increasing the in vivo susceptibility of mycobacteria to antimicrobial drugs.

21. A normally pathogenic mycobacterium, whose pathogenicity is mediated in all or in part by the presence or the expression of a polypeptide as defined in any one of claims 1 to 3 or a polypeptide which comprises a sequence selected from the sequences of Seq.ID.No: 31, 33, 35, 37 and 39 or a polypeptide substantially homogolous thereto, which mycobacterium harbours an attenuating mutation in a gene encoding one of the said polypeptides.

22. A vaccine comprising a mycobacterium as claimed in claim 21.

23. A vaccine according to claim 22 wherein the mycobacteria is selected from *Mavs*, *Mptb* and *Mtb*.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

HERMON-TAYLOR et al.

Serial No. To Be Assigned — Atty Ref.: 117-323

Filed: Concurrently Herewith — Group: Not Yet Assigned

For: NOVEL POLYNUCLEOTIDES AND POLYPEPTIDES IN PATHOGENIC MYCOBACTERIA AND THEIR USE AS DIAGNOSTICS, VACCINES AND TARGETS FOR CHEMOTHERAPY — Examiner: Not Yet Assigned

* * * * * * * * * * *

November 6, 2000

Assistant Commissioner for Patents
Washington, DC 20231

SUBMISSION OF FORMAL DRAWINGS

Sir:

Enclosed herewith is one (1) sheet of formal, inked drawings for the above-identified application.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

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Reg. No. 36,663

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Telephone: (703) 816-4000
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Fig.1a)

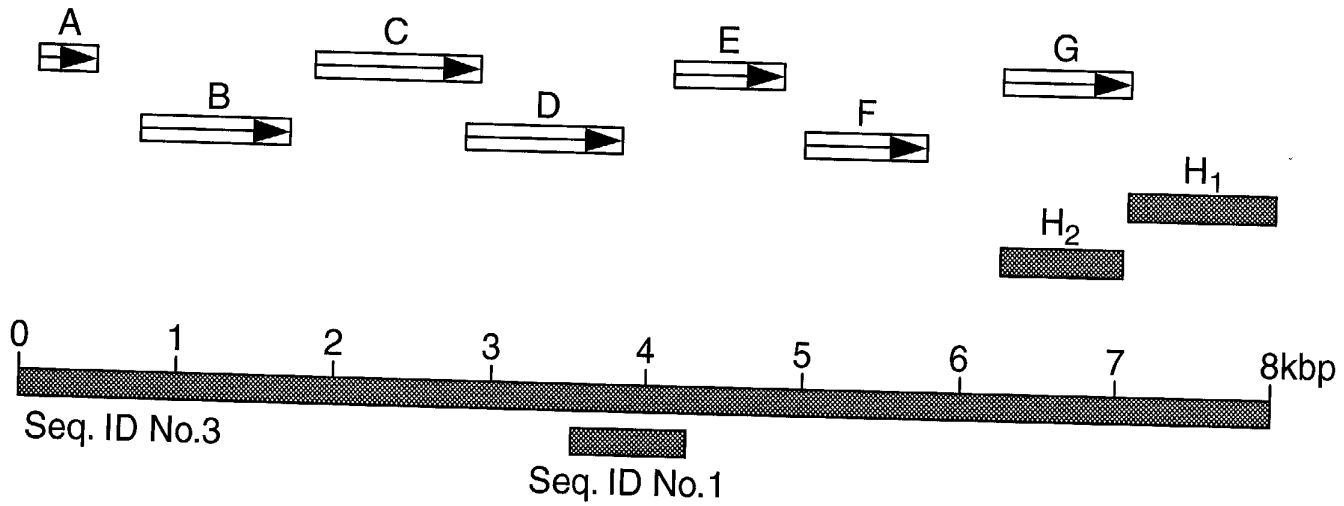
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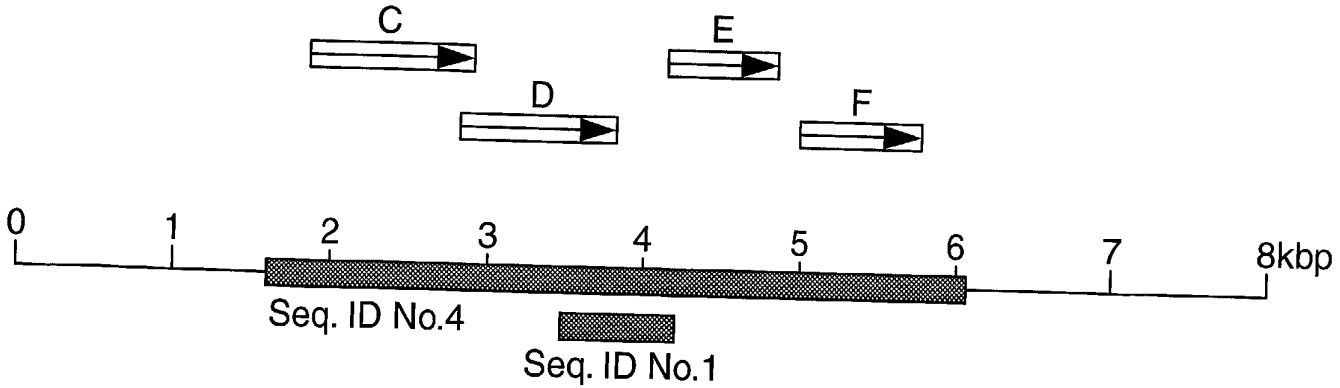
Fig.1b)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117-260
N.70283B DMG/IJB/ap

Nixon & Vanderhye P.C. (12/95)

RULE 63 (37 C.F.R. 1.63)
DECLARATION AND POWER OF ATTORNEY
FOR PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

I a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

NOVEL POLYNUCLEOTIDES AND POLYPEPTIDES IN PATHOGENIC MYCOBACTERIA AND THEIR USE AS DIAGNOSTICS, VACCINES AND TARGETS FOR CHEMOTHERAPY

the specification of which (check applicable box(s)):

☐ is attached hereto
☐ was filed on 19 June 1998 as U.S. Application Serial No. (To Be Assigned) (Atty Dkt. No. 117-260)
☒ was filed as PCT International application No. PCT/GB96/03221 on 23 December 1996
and (if applicable to U.S. or PCT application) was amended on 22 December 1997

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 35 U.S.C. 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed or, if no priority is claimed, before the filing date of this application:

Priority Foreign Application(s):

Application Number	Country	Day/Month/Year Filed
9526178.0	Great Britain	21 December 1995

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

Application Number	Date/Month/Year Filed

I hereby claim the benefit under 35 U.S.C. 120/365 of all prior United States and PCT International applications listed above or below and, insofar as the subject matter of each of the claims of this application is not disclosed in such prior applications in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose material information as defined in 37 C.F.R. 1.56 which occurred between the filing date of the prior applications and the national or PCT international filing date of this application:

Prior U.S./PCT Application(s): Application Serial No.	Day/Month/Year Filed	Status: patented pending, abandoned
PCT/GB96/03221	23 December 1996	

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon. And I hereby appoint **NIXON & VANDERHYE P.C., 1100 North Glebe Rd., 8th Floor, Arlington, VA 22201-4714, telephone number (703) 816-4000 (to whom all communications are to be directed)**, and the following attorneys thereof (of the same address) individually and collectively my attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent: Arthur R. Crawford, 25327; Larry S. Nixon, 25640; Robert A. Vanderhye, 27076; James T. Hosmer, 30184; Robert W. Faris, 31352; Richard G. Besha, 22770; Mark E. Nusbaum, 32348; Michael J. Keenan, 32106; Bryan H. Davidson, 30251; Stanley C. Spooner, 27393; Leonard C. Mitchard, 29009; Duane M. Byers, 33363; Jeffry H. Nelson, 30481; John R. Lastova, 33149; H. Warren Burnam, Jr. 29366; Thomas E. Byrne, 32205; Mary J. Wilson, 32955; J. Scott Davidson, 33489; Alan M. Kagen, 36178; William J. Griffin, 31260; Robert A. Molan, 29834; B. J. Sadoff, 36663; James D. Berquist, 34776; Updeep S. Gill, 37334.*

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FOR ADDITIONAL INVENTORS, check box ☒ and attach sheet with same information and signature and date for each.

117-260

RULE 63 (37 C.F.R. 1.63)
DECLARATION AND POWER OF ATTORNEY
FOR PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Nixon & Vanderhye P.C. (12/95)

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Post Office Address: _____
(Zip Code) _____

9. Inventor's Signature: _____ Date: _____
Inventor: (first) MI (last) (citizenship)
Residence: (city) _____ (state/country) _____
Post Office Address: _____
(Zip Code) _____

10. Inventor's Signature: _____ Date: _____
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Residence: (city) _____ (state/country) _____
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(Zip Code) _____

11. Inventor's Signature: _____ Date: _____
Inventor: (first) MI (last) (citizenship)
Residence: (city) _____ (state/country) _____
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(Zip Code) _____

SEQUENCE LISTING

<110> Hermon-Taylor, John
Doran, Tim
Millar, Douglas
Tizard, Mark
Loughlin, Mark
Sumar, Nazira

<120> NOVEL POLYNUCLEOTIDES AND POLYPEPTIDES IN PATHOGENIC MYCOBACTERIA AND THEIR USE AS DIAGNOSTICS, VACCINES AND TARGETS FOR CHEMOTHERAPY

<130> 117-260

<140> 09/091,538
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tacgcggttg ataagggtta aggccgtctc caaagaacga agcgcagaac cgtagtcgcg 4140

gatccacatt ggacttcttt aacgcgtttg cgtcctgatc cacctttcaa ccccgttccg 4200

cgtgacgcgg cgcgcagaga gtggtcgcat atcgcgtcac tgttctcgtg ccagtgcttg 4260

gaaagcgtcg agcactctgg ttcgcgttct tgacgttcgc gcccgcccct agaggtagcg 4320

tgtcacgtga ctgaagccaa tgagtgcaac tcggcgtcgc gaaaggtttc agtcgcggtt 4380

gagcaagaca ccgcaagact actggagtgc gtgcacaagc gcctccagct cacgg 4435

<210> 5
<211> 378
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(375)

<400> 5

```
atg atc gct gtg atc tgg tcg gcg gtg ccg aca gga acc gtc gac ttg   48
Met Ile Ala Val Ile Trp Ser Ala Val Pro Thr Gly Thr Val Asp Leu
  1               5                  10                  15

tcg acg atc acc ttg tac cgg tcg atg tat gac cca atg tcg tcc gca   96
Ser Thr Ile Thr Leu Tyr Arg Ser Met Tyr Asp Pro Met Ser Ser Ala
            20                  25                  30

acc gag aag acg tac gtc agg tcc gcc gcc ccg ctt tca ccc atg ggc   144
Thr Glu Lys Thr Tyr Val Arg Ser Ala Ala Pro Leu Ser Pro Met Gly
        35                  40                  45

gtc ggg acg gcg atg aaa atg acg tcc gcg tgc tcg att ccg cgt tgc   192
Val Gly Thr Ala Met Lys Met Thr Ser Ala Cys Ser Ile Pro Arg Cys
    50                  55                  60

cgg tcg gtg gtg aag tca atc agc ccg ttc tca cgg ttc ctc gca atc   240
Arg Ser Val Val Lys Ser Ile Ser Pro Phe Ser Arg Phe Leu Ala Ile
65                  70                  75                  80
```

```
aac tcc caa ccc ggg ctc gaa aat cgg gac act gcc tgc gag gag caa   288
Asn Ser Gln Pro Gly Leu Glu Asn Arg Asp Thr Ala Cys Glu Glu Gln
                 85                  90                  95

atc gat ctt ggc ctg atc gat atc gac aca gac gac atc gtt gcc gct   336
Ile Asp Leu Gly Leu Ile Asp Ile Asp Thr Asp Asp Ile Val Ala Ala
            100                 105                 110

atc cgc gag aca ggc gcc cgt gac gag gcc tac ata gcc tga           378
Ile Arg Glu Thr Gly Ala Arg Asp Glu Ala Tyr Ile Ala
        115                 120                 125
```

<210> 6
<211> 125
<212> PRT
<213> Mycobacterium

<400> 6

```
Met Ile Ala Val Ile Trp Ser Ala Val Pro Thr Gly Thr Val Asp Leu
  1               5                  10                  15

Ser Thr Ile Thr Leu Tyr Arg Ser Met Tyr Asp Pro Met Ser Ser Ala
             20                  25                  30

Thr Glu Lys Thr Tyr Val Arg Ser Ala Ala Pro Leu Ser Pro Met Gly
         35                  40                  45

Val Gly Thr Ala Met Lys Met Thr Ser Ala Cys Ser Ile Pro Arg Cys
     50                  55                  60

Arg Ser Val Val Lys Ser Ile Ser Pro Phe Ser Arg Phe Leu Ala Ile
 65                  70                  75                  80

Asn Ser Gln Pro Gly Leu Glu Asn Arg Asp Thr Ala Cys Glu Glu Gln
                 85                  90                  95

Ile Asp Leu Gly Leu Ile Asp Ile Asp Thr Asp Asp Ile Val Ala Ala
            100                 105                 110

Ile Arg Glu Thr Gly Ala Arg Asp Glu Ala Tyr Ile Ala
        115                 120                 125
```

<210> 7
<211> 834
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(831)

<400> 7

```
gtg tca tct gct cca acc gtg tcg gtg ata acg att tcg ctg aac gat   48
Val Ser Ser Ala Pro Thr Val Ser Val Ile Thr Ile Ser Leu Asn Asp
  1               5                  10                  15
```

```
ctc gag gga ttg aaa agc acc gtg gag agc gtt cgc gcg cag cgc tat   96
Leu Glu Gly Leu Lys Ser Thr Val Glu Ser Val Arg Ala Gln Arg Tyr
            20                  25                  30

ggg ggg cga atc gag cac atc gtc atc gac ggt gga tcg ggc gac gcc  144
Gly Gly Arg Ile Glu His Ile Val Ile Asp Gly Gly Ser Gly Asp Ala
        35                  40                  45

gtc gtg gag tat ctg tcc ggc gat cct ggc ttt gca tat tgg caa tct  192
Val Val Glu Tyr Leu Ser Gly Asp Pro Gly Phe Ala Tyr Trp Gln Ser
    50                  55                  60

cag ccc gac aac ggg aga tat gac gcg atg aat cag ggc att gcc cat  240
Gln Pro Asp Asn Gly Arg Tyr Asp Ala Met Asn Gln Gly Ile Ala His
65                  70                  75                  80

tcg tcg ggc gac ctg ttg tgg ttt atg cac tcc acg gat cgt ttc tcc  288
Ser Ser Gly Asp Leu Leu Trp Phe Met His Ser Thr Asp Arg Phe Ser
                85                  90                  95

gat cca gat gca gtc gct tcc gtg gtg gag gcg ctc tcg ggg cat gga  336
Asp Pro Asp Ala Val Ala Ser Val Val Glu Ala Leu Ser Gly His Gly
            100                 105                 110

cca gta cgt gat ttg tgg ggt tac ggg aaa aac aac ctt gtc gga ctc  384
Pro Val Arg Asp Leu Trp Gly Tyr Gly Lys Asn Asn Leu Val Gly Leu
        115                 120                 125

gac ggc aaa cca ctt ttc cct cgg ccg tac ggc tat atg ccg ttt aag  432
Asp Gly Lys Pro Leu Phe Pro Arg Pro Tyr Gly Tyr Met Pro Phe Lys
    130                 135                 140

atg cgg aaa ttt ctg ctc ggc gcg acg gtt gcg cat cag gcg aca ttc  480
Met Arg Lys Phe Leu Leu Gly Ala Thr Val Ala His Gln Ala Thr Phe
145                 150                 155                 160

ttc ggc gcg tcg ctg gta gcc aag ttg ggc ggt tac gat ctt gat ttt  528
Phe Gly Ala Ser Leu Val Ala Lys Leu Gly Gly Tyr Asp Leu Asp Phe
                165                 170                 175

gga ctc gag gcg gac cag ctg ttc atc tac cgt gcc gca cta ata cgg  576
Gly Leu Glu Ala Asp Gln Leu Phe Ile Tyr Arg Ala Ala Leu Ile Arg
            180                 185                 190

cct ccc gtc acg atc gac cgc gtg gtt tgc gac ttc gat gtc acg gga  624
Pro Pro Val Thr Ile Asp Arg Val Val Cys Asp Phe Asp Val Thr Gly
        195                 200                 205

cct ggt tca acc cag ccc atc cgt gag cac tat cgg acc ctg cgg cgg  672
Pro Gly Ser Thr Gln Pro Ile Arg Glu His Tyr Arg Thr Leu Arg Arg
    210                 215                 220

ctc tgg gac ctg cat ggc gac tac ccg ctg ggt ggg cgc aga gtg tcg  720
Leu Trp Asp Leu His Gly Asp Tyr Pro Leu Gly Gly Arg Arg Val Ser
225                 230                 235                 240

tgg gct tac ttg cgt gtg aag gag tac ttg att cgg gcc gac ctg gcc  768
Trp Ala Tyr Leu Arg Val Lys Glu Tyr Leu Ile Arg Ala Asp Leu Ala
                245                 250                 255
```

```
gca ttc aac gcg gta aag ttc ttg cga gcg aag ttc gcc aga gct tcg   816
Ala Phe Asn Ala Val Lys Phe Leu Arg Ala Lys Phe Ala Arg Ala Ser
            260                 265                 270

cgg aag caa aat tca tag                                          834
Arg Lys Gln Asn Ser
        275
```

<210> 8
<211> 277
<212> PRT
<213> Mycobacterium

<400> 8

```
Val Ser Ser Ala Pro Thr Val Ser Val Ile Thr Ile Ser Leu Asn Asp
  1               5                  10                  15

Leu Glu Gly Leu Lys Ser Thr Val Glu Ser Val Arg Ala Gln Arg Tyr
             20                  25                  30

Gly Gly Arg Ile Glu His Ile Val Ile Asp Gly Gly Ser Gly Asp Ala
         35                  40                  45

Val Val Glu Tyr Leu Ser Gly Asp Pro Gly Phe Ala Tyr Trp Gln Ser
     50                  55                  60

Gln Pro Asp Asn Gly Arg Tyr Asp Ala Met Asn Gln Gly Ile Ala His
 65                  70                  75                  80

Ser Ser Gly Asp Leu Leu Trp Phe Met His Ser Thr Asp Arg Phe Ser
                 85                  90                  95

Asp Pro Asp Ala Val Ala Ser Val Val Glu Ala Leu Ser Gly His Gly
            100                 105                 110

Pro Val Arg Asp Leu Trp Gly Tyr Gly Lys Asn Asn Leu Val Gly Leu
        115                 120                 125

Asp Gly Lys Pro Leu Phe Pro Arg Pro Tyr Gly Tyr Met Pro Phe Lys
    130                 135                 140

Met Arg Lys Phe Leu Leu Gly Ala Thr Val Ala His Gln Ala Thr Phe
145                 150                 155                 160

Phe Gly Ala Ser Leu Val Ala Lys Leu Gly Gly Tyr Asp Leu Asp Phe
                165                 170                 175

Gly Leu Glu Ala Asp Gln Leu Phe Ile Tyr Arg Ala Ala Leu Ile Arg
            180                 185                 190

Pro Pro Val Thr Ile Asp Arg Val Val Cys Asp Phe Asp Val Thr Gly
        195                 200                 205

Pro Gly Ser Thr Gln Pro Ile Arg Glu His Tyr Arg Thr Leu Arg Arg
    210                 215                 220

Leu Trp Asp Leu His Gly Asp Tyr Pro Leu Gly Gly Arg Arg Val Ser
225                 230                 235                 240
```

```
Trp Ala Tyr Leu Arg Val Lys Glu Tyr Leu Ile Arg Ala Asp Leu Ala
                245                 250                 255

Ala Phe Asn Ala Val Lys Phe Leu Arg Ala Lys Phe Ala Arg Ala Ser
            260                 265                 270

Arg Lys Gln Asn Ser
        275
```

<210> 9
<211> 1032
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(1029)

<400> 9

```
gtg aag cga gcg ctt ata aca ggg atc acg ggg cag gat ggt tcc tac   48
Val Lys Arg Ala Leu Ile Thr Gly Ile Thr Gly Gln Asp Gly Ser Tyr
  1               5                  10                  15

ctc gcc gag cta cta ctg agc aag gga tac gag gtt cac ggg ctc gtt   96
Leu Ala Glu Leu Leu Leu Ser Lys Gly Tyr Glu Val His Gly Leu Val
             20                  25                  30

cgt cga gct tcg acg ttt aac acg tcg cgg atc gat cac ctc tac gtt  144
Arg Arg Ala Ser Thr Phe Asn Thr Ser Arg Ile Asp His Leu Tyr Val
         35                  40                  45

gac cca cac caa ccg ggc gcg cgc ttg ttc ttg cac tat gca gac ctc  192
Asp Pro His Gln Pro Gly Ala Arg Leu Phe Leu His Tyr Ala Asp Leu
     50                  55                  60

act gac ggc acc cgg ttg gtg acc ctg ctc agc agt atc gac ccg gat  240
Thr Asp Gly Thr Arg Leu Val Thr Leu Leu Ser Ser Ile Asp Pro Asp
 65                  70                  75                  80

gag gtc tac aac ctc gca gcg cag tcc cat gtg cgc gtc agc ttt gac  288
Glu Val Tyr Asn Leu Ala Ala Gln Ser His Val Arg Val Ser Phe Asp
                85                  90                  95

gag cca gtg cat acc gga gac acc acc ggc atg gga tcg atc cga ctt  336
Glu Pro Val His Thr Gly Asp Thr Thr Gly Met Gly Ser Ile Arg Leu
            100                 105                 110

ctg gaa gca gtc cgc ctt tct cgg gtg gac tgc cgg ttc tat cag gct  384
Leu Glu Ala Val Arg Leu Ser Arg Val Asp Cys Arg Phe Tyr Gln Ala
        115                 120                 125

tcc tcg tcg gag atg ttc ggc gca tct ccg cca ccg cag aac gaa tcg  432
Ser Ser Ser Glu Met Phe Gly Ala Ser Pro Pro Pro Gln Asn Glu Ser
    130                 135                 140

acg ccg ttc tat ccc cgt tcg cca tac ggc gcg gcc aag gtc ttc tcg  480
Thr Pro Phe Tyr Pro Arg Ser Pro Tyr Gly Ala Ala Lys Val Phe Ser
145                 150                 155                 160
```

```
tac tgg acg act cgc aac tat cga gag gcg tac gga tta ttc gca gtg   528
Tyr Trp Thr Thr Arg Asn Tyr Arg Glu Ala Tyr Gly Leu Phe Ala Val
                165                 170                 175

aat ggc atc ttg ttc aac cat gag tcc ccc cgg cgc ggc gag act ttc   576
Asn Gly Ile Leu Phe Asn His Glu Ser Pro Arg Arg Gly Glu Thr Phe
            180                 185                 190

gtg acc cga aag atc acg cgt gcc gtg gcg cgc atc cga gct ggc gtc   624
Val Thr Arg Lys Ile Thr Arg Ala Val Ala Arg Ile Arg Ala Gly Val
        195                 200                 205

caa tcg gag gtc tat atg ggc aac ctc gat gcg atc cgc gac tgg ggc   672
Gln Ser Glu Val Tyr Met Gly Asn Leu Asp Ala Ile Arg Asp Trp Gly
    210                 215                 220

tac gcg ccc gaa tat gtc gag ggg atg tgg agg atg ttg caa gcg cct   720
Tyr Ala Pro Glu Tyr Val Glu Gly Met Trp Arg Met Leu Gln Ala Pro
225                 230                 235                 240

gaa cct gat gac tac gtc ctg gcg aca ggg cgt ggt tac acc gta cgt   768
Glu Pro Asp Asp Tyr Val Leu Ala Thr Gly Arg Gly Tyr Thr Val Arg
                245                 250                 255

gag ttc gct caa gct gct ttt gac cat gtc ggg ctc gac tgg caa aag   816
Glu Phe Ala Gln Ala Ala Phe Asp His Val Gly Leu Asp Trp Gln Lys
            260                 265                 270

cgc gtc aag ttt gac gac cgc tat ttg cgt ccc acc gag gtc gat tcg   864
Arg Val Lys Phe Asp Asp Arg Tyr Leu Arg Pro Thr Glu Val Asp Ser
        275                 280                 285

cta gta gga gat gcc gac aag gcg gcc cag tca ctc ggc tgg aaa gct   912
Leu Val Gly Asp Ala Asp Lys Ala Ala Gln Ser Leu Gly Trp Lys Ala
    290                 295                 300

tcg gtt cat act ggt gaa ctc gcg cgc atc atg gtg gac gcg gac atc   960
Ser Val His Thr Gly Glu Leu Ala Arg Ile Met Val Asp Ala Asp Ile
305                 310                 315                 320

gcc gcg ttg gag tgc gat ggc aca cca tgg atc gac acg ccg atg ttg   1008
Ala Ala Leu Glu Cys Asp Gly Thr Pro Trp Ile Asp Thr Pro Met Leu
                325                 330                 335

cct ggt tgg ggc aga gta agt tga                                   1032
Pro Gly Trp Gly Arg Val Ser
            340
```

<210> 10
<211> 343
<212> PRT
<213> Mycobacterium

<400> 10

```
Val Lys Arg Ala Leu Ile Thr Gly Ile Thr Gly Gln Asp Gly Ser Tyr
  1               5                  10                  15

Leu Ala Glu Leu Leu Leu Ser Lys Gly Tyr Glu Val His Gly Leu Val
             20                  25                  30
```

```
Arg Arg Ala Ser Thr Phe Asn Thr Ser Arg Ile Asp His Leu Tyr Val
        35                  40                  45

Asp Pro His Gln Pro Gly Ala Arg Leu Phe Leu His Tyr Ala Asp Leu
    50                  55                  60

Thr Asp Gly Thr Arg Leu Val Thr Leu Leu Ser Ser Ile Asp Pro Asp
65                  70                  75                  80

Glu Val Tyr Asn Leu Ala Ala Gln Ser His Val Arg Val Ser Phe Asp
                85                  90                  95

Glu Pro Val His Thr Gly Asp Thr Thr Gly Met Gly Ser Ile Arg Leu
            100                 105                 110

Leu Glu Ala Val Arg Leu Ser Arg Val Asp Cys Arg Phe Tyr Gln Ala
        115                 120                 125

Ser Ser Ser Glu Met Phe Gly Ala Ser Pro Pro Pro Gln Asn Glu Ser
    130                 135                 140

Thr Pro Phe Tyr Pro Arg Ser Pro Tyr Gly Ala Ala Lys Val Phe Ser
145                 150                 155                 160

Tyr Trp Thr Thr Arg Asn Tyr Arg Glu Ala Tyr Gly Leu Phe Ala Val
                165                 170                 175

Asn Gly Ile Leu Phe Asn His Glu Ser Pro Arg Arg Gly Glu Thr Phe
            180                 185                 190

Val Thr Arg Lys Ile Thr Arg Ala Val Ala Arg Ile Arg Ala Gly Val
        195                 200                 205

Gln Ser Glu Val Tyr Met Gly Asn Leu Asp Ala Ile Arg Asp Trp Gly
    210                 215                 220

Tyr Ala Pro Glu Tyr Val Glu Gly Met Trp Arg Met Leu Gln Ala Pro
225                 230                 235                 240

Glu Pro Asp Asp Tyr Val Leu Ala Thr Gly Arg Gly Tyr Thr Val Arg
                245                 250                 255

Glu Phe Ala Gln Ala Ala Phe Asp His Val Gly Leu Asp Trp Gln Lys
            260                 265                 270

Arg Val Lys Phe Asp Asp Arg Tyr Leu Arg Pro Thr Glu Val Asp Ser
        275                 280                 285

Leu Val Gly Asp Ala Asp Lys Ala Ala Gln Ser Leu Gly Trp Lys Ala
    290                 295                 300

Ser Val His Thr Gly Glu Leu Ala Arg Ile Met Val Asp Ala Asp Ile
305                 310                 315                 320

Ala Ala Leu Glu Cys Asp Gly Thr Pro Trp Ile Asp Thr Pro Met Leu
                325                 330                 335

Pro Gly Trp Gly Arg Val Ser
            340
```

<210> 11
<211> 1032
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(1029)

<400> 11

```
gtg aag cga gcg ctt ata aca ggg atc acg ggg cag gat ggt tcc tac   48
Val Lys Arg Ala Leu Ile Thr Gly Ile Thr Gly Gln Asp Gly Ser Tyr
  1               5                  10                  15

ctc gcc gag cta cta ctg agc aag gga tac gag gtt cac ggg ctc gtt   96
Leu Ala Glu Leu Leu Leu Ser Lys Gly Tyr Glu Val His Gly Leu Val
            20                  25                  30

cgt cga gct tcg acg ttt aac acg tcg cgg atc gat cac ctc tac gtt   144
Arg Arg Ala Ser Thr Phe Asn Thr Ser Arg Ile Asp His Leu Tyr Val
         35                  40                  45

gac cca cac caa ccg ggc gcg cgc ttg ttc ttg cac tat gca gac ctc   192
Asp Pro His Gln Pro Gly Ala Arg Leu Phe Leu His Tyr Ala Asp Leu
     50                  55                  60

act gac ggc acc cgg ttg gtg acc ctg ctc agc agt atc gac ccg gat   240
Thr Asp Gly Thr Arg Leu Val Thr Leu Leu Ser Ser Ile Asp Pro Asp
 65                  70                  75                  80

gag gtc tac aac ctc gca gcg cag tcc cat gtg cgc gtc agc ttt gac   288
Glu Val Tyr Asn Leu Ala Ala Gln Ser His Val Arg Val Ser Phe Asp
                85                  90                  95

gag cca gtg cat acc gga gac acc acc ggc atg gga tcg atc cga ctt   336
Glu Pro Val His Thr Gly Asp Thr Thr Gly Met Gly Ser Ile Arg Leu
            100                 105                 110

ctg gaa gca gtc cgc ctt tct cgg gtg gac tgc cgg ttc tat cag gct   384
Leu Glu Ala Val Arg Leu Ser Arg Val Asp Cys Arg Phe Tyr Gln Ala
        115                 120                 125

tcc tcg tcg gag atg ttc ggc gca tct ccg cca ccg cag aac gaa tcg   432
Ser Ser Ser Glu Met Phe Gly Ala Ser Pro Pro Pro Gln Asn Glu Ser
    130                 135                 140

acg ccg ttc tat ccc cgt tcg cca tac ggc gcg gcc aag gtc ttc tcg   480
Thr Pro Phe Tyr Pro Arg Ser Pro Tyr Gly Ala Ala Lys Val Phe Ser
145                 150                 155                 160

tac tgg acg act cgc aac tat cga gag gcg tac gga tta ttc gca gtg   528
Tyr Trp Thr Thr Arg Asn Tyr Arg Glu Ala Tyr Gly Leu Phe Ala Val
                165                 170                 175

aat ggc atc ttg ttc aac cat gag tcc ccc cgg cgc ggc gag act ttc   576
Asn Gly Ile Leu Phe Asn His Glu Ser Pro Arg Arg Gly Glu Thr Phe
            180                 185                 190

gtg acc cga aag atc acg cgt gcc gtg gcg cgc atc cga gct ggc gtc   624
Val Thr Arg Lys Ile Thr Arg Ala Val Ala Arg Ile Arg Ala Gly Val
        195                 200                 205
```

```
caa tcg gag gtc tat atg ggc aac ctc gat gcg atc cgc gac tgg ggc   672
Gln Ser Glu Val Tyr Met Gly Asn Leu Asp Ala Ile Arg Asp Trp Gly
    210                 215                 220

tac gcg ccc gaa tat gtc gag ggg atg tgg agg atg ttg caa gcg cct   720
Tyr Ala Pro Glu Tyr Val Glu Gly Met Trp Arg Met Leu Gln Ala Pro
225                 230                 235                 240

gaa cct gat gac tac gtc ctg gcg aca ggg cgt ggt tac acc gta cgt   768
Glu Pro Asp Asp Tyr Val Leu Ala Thr Gly Arg Gly Tyr Thr Val Arg
                245                 250                 255

gag ttc gct caa gct gct ttt gac cac gtc ggg ctc gac tgg caa aag   816
Glu Phe Ala Gln Ala Ala Phe Asp His Val Gly Leu Asp Trp Gln Lys
            260                 265                 270

cac gtc aag ttt gac gac cgc tat ttg cgc ccc acc gag gtc gat tcg   864
His Val Lys Phe Asp Asp Arg Tyr Leu Arg Pro Thr Glu Val Asp Ser
        275                 280                 285

cta gta gga gat gcc gac agg gcg gcc cag tca ctc ggc tgg aaa gct   912
Leu Val Gly Asp Ala Asp Arg Ala Ala Gln Ser Leu Gly Trp Lys Ala
    290                 295                 300

tcg gtt cat act ggt gaa ctc gcg cgc atc atg gtg gac gcg gac atc   960
Ser Val His Thr Gly Glu Leu Ala Arg Ile Met Val Asp Ala Asp Ile
305                 310                 315                 320

gcc gcg tcg gag tgc gat ggc aca cca tgg atc gac acg ccg atg ttg  1008
Ala Ala Ser Glu Cys Asp Gly Thr Pro Trp Ile Asp Thr Pro Met Leu
                325                 330                 335

cct ggt tgg ggc gga gta agt tga                                 1032
Pro Gly Trp Gly Gly Val Ser
            340
```

<210> 12
<211> 343
<212> PRT
<213> Mycobacterium

<400> 12

```
Val Lys Arg Ala Leu Ile Thr Gly Ile Thr Gly Gln Asp Gly Ser Tyr
  1               5                  10                  15

Leu Ala Glu Leu Leu Leu Ser Lys Gly Tyr Glu Val His Gly Leu Val
             20                  25                  30

Arg Arg Ala Ser Thr Phe Asn Thr Ser Arg Ile Asp His Leu Tyr Val
         35                  40                  45

Asp Pro His Gln Pro Gly Ala Arg Leu Phe Leu His Tyr Ala Asp Leu
     50                  55                  60

Thr Asp Gly Thr Arg Leu Val Thr Leu Leu Ser Ser Ile Asp Pro Asp
 65                  70                  75                  80

Glu Val Tyr Asn Leu Ala Ala Gln Ser His Val Arg Val Ser Phe Asp
                 85                  90                  95
```

```
Glu Pro Val His Thr Gly Asp Thr Thr Gly Met Gly Ser Ile Arg Leu
            100                 105                 110

Leu Glu Ala Val Arg Leu Ser Arg Val Asp Cys Arg Phe Tyr Gln Ala
        115                 120                 125

Ser Ser Ser Glu Met Phe Gly Ala Ser Pro Pro Pro Gln Asn Glu Ser
    130                 135                 140

Thr Pro Phe Tyr Pro Arg Ser Pro Tyr Gly Ala Ala Lys Val Phe Ser
145                 150                 155                 160

Tyr Trp Thr Thr Arg Asn Tyr Arg Glu Ala Tyr Gly Leu Phe Ala Val
                165                 170                 175

Asn Gly Ile Leu Phe Asn His Glu Ser Pro Arg Arg Gly Glu Thr Phe
            180                 185                 190

Val Thr Arg Lys Ile Thr Arg Ala Val Ala Arg Ile Arg Ala Gly Val
        195                 200                 205

Gln Ser Glu Val Tyr Met Gly Asn Leu Asp Ala Ile Arg Asp Trp Gly
    210                 215                 220

Tyr Ala Pro Glu Tyr Val Glu Gly Met Trp Arg Met Leu Gln Ala Pro
225                 230                 235                 240

Glu Pro Asp Asp Tyr Val Leu Ala Thr Gly Arg Gly Tyr Thr Val Arg
                245                 250                 255

Glu Phe Ala Gln Ala Ala Phe Asp His Val Gly Leu Asp Trp Gln Lys
            260                 265                 270

His Val Lys Phe Asp Asp Arg Tyr Leu Arg Pro Thr Glu Val Asp Ser
        275                 280                 285

Leu Val Gly Asp Ala Asp Arg Ala Ala Gln Ser Leu Gly Trp Lys Ala
    290                 295                 300

Ser Val His Thr Gly Glu Leu Ala Arg Ile Met Val Asp Ala Asp Ile
305                 310                 315                 320

Ala Ala Ser Glu Cys Asp Gly Thr Pro Trp Ile Asp Thr Pro Met Leu
                325                 330                 335

Pro Gly Trp Gly Gly Val Ser
            340
```

<210> 13
<211> 1020
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(1017)

```
<400> 13
gtg cga tgg cac acc atg gat cga cac gcc gat gtt gcc tgg ttg ggg      48
Val Arg Trp His Thr Met Asp Arg His Ala Asp Val Ala Trp Leu Gly
 1               5                  10                  15

cag agt aag ttg acg act aca cct ggg cct ctg gac cgc gca acg ccc      96
Gln Ser Lys Leu Thr Thr Thr Pro Gly Pro Leu Asp Arg Ala Thr Pro
            20                  25                  30

gtg tat atc gcc ggt cat cgg ggg ctg gtc ggc tca gcg ctc gta cgt     144
Val Tyr Ile Ala Gly His Arg Gly Leu Val Gly Ser Ala Leu Val Arg
        35                  40                  45

aga ttt gag gcc gag ggg ttc acc aat ctc att gtg cga tca cgc gat     192
Arg Phe Glu Ala Glu Gly Phe Thr Asn Leu Ile Val Arg Ser Arg Asp
    50                  55                  60

gag att gat ctg acg gac cga gcc gca acg ttt gat ttt gtg tct gag     240
Glu Ile Asp Leu Thr Asp Arg Ala Ala Thr Phe Asp Phe Val Ser Glu
65                  70                  75                  80

aca aga cca cag gtg atc atc gat gcg gcc gca cgg gtc ggc ggc atc     288
Thr Arg Pro Gln Val Ile Ile Asp Ala Ala Ala Arg Val Gly Gly Ile
                85                  90                  95

atg gcg aat aac acc tat ccc gcg gac ttc ttg tcc gaa aac ctc cga     336
Met Ala Asn Asn Thr Tyr Pro Ala Asp Phe Leu Ser Glu Asn Leu Arg
            100                 105                 110

atc cag acc aat ttg ctc gac gca gct gtc gcc gtg cgt gtg ccg cgg     384
Ile Gln Thr Asn Leu Leu Asp Ala Ala Val Ala Val Arg Val Pro Arg
        115                 120                 125

ctc ctt ttc ctc ggt tcg tca tgc atc tac ccg aag tac gct ccg caa     432
Leu Leu Phe Leu Gly Ser Ser Cys Ile Tyr Pro Lys Tyr Ala Pro Gln
    130                 135                 140

cct atc cac gag agt gct tta ttg act ggc cct ttg gag ccc acc aac     480
Pro Ile His Glu Ser Ala Leu Leu Thr Gly Pro Leu Glu Pro Thr Asn
145                 150                 155                 160

gac gcg tat gcg atc gcc aag atc gcc ggt atc ctg caa gtt cag gcg     528
Asp Ala Tyr Ala Ile Ala Lys Ile Ala Gly Ile Leu Gln Val Gln Ala
                165                 170                 175

gtt agg cgc caa tat ggg ctg gcg tgg atc tct gcg atg ccg act aac     576
Val Arg Arg Gln Tyr Gly Leu Ala Trp Ile Ser Ala Met Pro Thr Asn
            180                 185                 190

ctc tac gga ccc ggc gac aac ttc tcc ccg tcc ggg tcg cat ctc ttg     624
Leu Tyr Gly Pro Gly Asp Asn Phe Ser Pro Ser Gly Ser His Leu Leu
        195                 200                 205

ccg gcg ctc atc cgt cga tat gag gaa gcc aaa gct ggt ggt gca gaa     672
Pro Ala Leu Ile Arg Arg Tyr Glu Glu Ala Lys Ala Gly Gly Ala Glu
    210                 215                 220

gag gtg acg aat tgg ggg acc ggt act ccg cgg cgc gaa ctt ctg cat     720
Glu Val Thr Asn Trp Gly Thr Gly Thr Pro Arg Arg Glu Leu Leu His
225                 230                 235                 240
```

```
gtc gac gat ctg gcg agc gca tgc ctg ttc ctt ttg gaa cat ttc gat   768
Val Asp Asp Leu Ala Ser Ala Cys Leu Phe Leu Leu Glu His Phe Asp
                245                 250                 255

ggt ccg aac cac gtc aac gtg ggc acc ggc gtc gat cac agc att agc   816
Gly Pro Asn His Val Asn Val Gly Thr Gly Val Asp His Ser Ile Ser
            260                 265                 270

gag atc gca gac atg gtc gct aca gcg gtg ggc tac atc ggc gaa aca   864
Glu Ile Ala Asp Met Val Ala Thr Ala Val Gly Tyr Ile Gly Glu Thr
        275                 280                 285

cgt tgg gat cca act aaa ccc gat gga acc ccg cgc aaa cta ttg gac   912
Arg Trp Asp Pro Thr Lys Pro Asp Gly Thr Pro Arg Lys Leu Leu Asp
    290                 295                 300

gtc tcc gcg cta cgc gag ttg ggt tgg cgc ccg cga atc gca ctg aaa   960
Val Ser Ala Leu Arg Glu Leu Gly Trp Arg Pro Arg Ile Ala Leu Lys
305                 310                 315                 320

gac ggc atc gat gca acg gtg tcg tgg tac cgc aca aat gcc gat gcc  1008
Asp Gly Ile Asp Ala Thr Val Ser Trp Tyr Arg Thr Asn Ala Asp Ala
                325                 330                 335

gtg agg agg taa                                                 1020
Val Arg Arg
```

<210> 14
<211> 339
<212> PRT
<213> Mycobacterium

<400> 14

```
Val Arg Trp His Thr Met Asp Arg His Ala Asp Val Ala Trp Leu Gly
  1               5                  10                  15

Gln Ser Lys Leu Thr Thr Thr Pro Gly Pro Leu Asp Arg Ala Thr Pro
             20                  25                  30

Val Tyr Ile Ala Gly His Arg Gly Leu Val Gly Ser Ala Leu Val Arg
         35                  40                  45

Arg Phe Glu Ala Glu Gly Phe Thr Asn Leu Ile Val Arg Ser Arg Asp
     50                  55                  60

Glu Ile Asp Leu Thr Asp Arg Ala Ala Thr Phe Asp Phe Val Ser Glu
 65                  70                  75                  80

Thr Arg Pro Gln Val Ile Ile Asp Ala Ala Ala Arg Val Gly Gly Ile
                 85                  90                  95

Met Ala Asn Asn Thr Tyr Pro Ala Asp Phe Leu Ser Glu Asn Leu Arg
            100                 105                 110

Ile Gln Thr Asn Leu Leu Asp Ala Ala Val Ala Val Arg Val Pro Arg
        115                 120                 125

Leu Leu Phe Leu Gly Ser Ser Cys Ile Tyr Pro Lys Tyr Ala Pro Gln
    130                 135                 140
```

```
Pro Ile His Glu Ser Ala Leu Leu Thr Gly Pro Leu Glu Pro Thr Asn
145                 150                 155                 160

Asp Ala Tyr Ala Ile Ala Lys Ile Ala Gly Ile Leu Gln Val Gln Ala
                165                 170                 175

Val Arg Arg Gln Tyr Gly Leu Ala Trp Ile Ser Ala Met Pro Thr Asn
            180                 185                 190

Leu Tyr Gly Pro Gly Asp Asn Phe Ser Pro Ser Gly Ser His Leu Leu
        195                 200                 205

Pro Ala Leu Ile Arg Arg Tyr Glu Glu Ala Lys Ala Gly Gly Ala Glu
    210                 215                 220

Glu Val Thr Asn Trp Gly Thr Gly Thr Pro Arg Arg Glu Leu Leu His
225                 230                 235                 240

Val Asp Asp Leu Ala Ser Ala Cys Leu Phe Leu Leu Glu His Phe Asp
                245                 250                 255

Gly Pro Asn His Val Asn Val Gly Thr Gly Val Asp His Ser Ile Ser
            260                 265                 270

Glu Ile Ala Asp Met Val Ala Thr Ala Val Gly Tyr Ile Gly Glu Thr
        275                 280                 285

Arg Trp Asp Pro Thr Lys Pro Asp Gly Thr Pro Arg Lys Leu Leu Asp
    290                 295                 300

Val Ser Ala Leu Arg Glu Leu Gly Trp Arg Pro Arg Ile Ala Leu Lys
305                 310                 315                 320

Asp Gly Ile Asp Ala Thr Val Ser Trp Tyr Arg Thr Asn Ala Asp Ala
                325                 330                 335

Val Arg Arg
```

<210> 15
<211> 1020
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(1017)

<400> 15

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gtg cga tgg cac acc atg gat cga cac gcc gat gtt gcc tgg ttg ggg   48
Val Arg Trp His Thr Met Asp Arg His Ala Asp Val Ala Trp Leu Gly
  1               5                  10                  15

cgg agt aag ttg acg act aca cct ggg cct ctg gac cgc gca acg ccc   96
Arg Ser Lys Leu Thr Thr Thr Pro Gly Pro Leu Asp Arg Ala Thr Pro
             20                  25                  30

gtg tat atc gcc ggt cat cgg ggg ctg gtc ggc tca gcg ctc gta cgt   144
Val Tyr Ile Ala Gly His Arg Gly Leu Val Gly Ser Ala Leu Val Arg
         35                  40                  45
```

```
aga ttt gag gcc gag ggg ttc acc aat ctc att gtg cga tca cgc gat   192
Arg Phe Glu Ala Glu Gly Phe Thr Asn Leu Ile Val Arg Ser Arg Asp
     50                  55                  60

gag att gat ctg acg gac cga gcc gca acg ttt gat ttt gtg tct gag   240
Glu Ile Asp Leu Thr Asp Arg Ala Ala Thr Phe Asp Phe Val Ser Glu
 65                  70                  75                  80

aca aga cca cag gtg atc atc gat gcg gcc gca cgg gtc ggc ggc atc   288
Thr Arg Pro Gln Val Ile Ile Asp Ala Ala Ala Arg Val Gly Gly Ile
                 85                  90                  95

atg gcg aat aac acc tat ccc gcg gac ttc ttg tcc gaa aac ctc cga   336
Met Ala Asn Asn Thr Tyr Pro Ala Asp Phe Leu Ser Glu Asn Leu Arg
            100                 105                 110

atc cag acc aat ttg ctc gac gca gct gtc gcc gtg cgt gtg ccg cgg   384
Ile Gln Thr Asn Leu Leu Asp Ala Ala Val Ala Val Arg Val Pro Arg
        115                 120                 125

ctc ctt ttc ctc ggt tcg tca tgc atc tac ccg aag tac gct ccg caa   432
Leu Leu Phe Leu Gly Ser Ser Cys Ile Tyr Pro Lys Tyr Ala Pro Gln
    130                 135                 140

cct atc cac gag agt gct tta ttg act ggc cct ttg gag ccc acc aac   480
Pro Ile His Glu Ser Ala Leu Leu Thr Gly Pro Leu Glu Pro Thr Asn
145                 150                 155                 160

gac gcg tat gcg atc gcc aag atc gcc ggt atc ctg caa gtt cag gcg   528
Asp Ala Tyr Ala Ile Ala Lys Ile Ala Gly Ile Leu Gln Val Gln Ala
                165                 170                 175

gtt agg cgc caa tat ggg ctg gcg tgg atc tct gcg atg ccg act aac   576
Val Arg Arg Gln Tyr Gly Leu Ala Trp Ile Ser Ala Met Pro Thr Asn
            180                 185                 190

ctc tac gga ccc ggc gac aac ttc tcc ccg tcc ggg tcg cat ctc ttg   624
Leu Tyr Gly Pro Gly Asp Asn Phe Ser Pro Ser Gly Ser His Leu Leu
        195                 200                 205

ccg gcg ctc atc cgt cga tat gag gaa gcc aaa gct ggt ggt gca gaa   672
Pro Ala Leu Ile Arg Arg Tyr Glu Glu Ala Lys Ala Gly Gly Ala Glu
    210                 215                 220

gag gtg acg aat tgg ggg acc ggt act ccg cgg cgc gaa ctt ctg cat   720
Glu Val Thr Asn Trp Gly Thr Gly Thr Pro Arg Arg Glu Leu Leu His
225                 230                 235                 240

gtc gac gat ctg gcg agc gca tgc ctg ttc ctt ttg gaa cat ttc gat   768
Val Asp Asp Leu Ala Ser Ala Cys Leu Phe Leu Leu Glu His Phe Asp
                245                 250                 255

ggt ccg aac cac gtc aac gtg ggc acc ggc gtc gat cac agc att agc   816
Gly Pro Asn His Val Asn Val Gly Thr Gly Val Asp His Ser Ile Ser
            260                 265                 270

gag atc gca gac atg gtc gct acg gcg gtg ggc tac atc ggc gaa aca   864
Glu Ile Ala Asp Met Val Ala Thr Ala Val Gly Tyr Ile Gly Glu Thr
        275                 280                 285
```

```
cgt tgg gat cca act aaa ccc gat gga acc ccg cgc aaa cta ttg gac   912
Arg Trp Asp Pro Thr Lys Pro Asp Gly Thr Pro Arg Lys Leu Leu Asp
    290                 295                 300

gtc tcc gcg cta cgc gag ttg ggt tgg cgc ccg cga atc gca ctg aaa   960
Val Ser Ala Leu Arg Glu Leu Gly Trp Arg Pro Arg Ile Ala Leu Lys
305                 310                 315                 320

gac ggc atc gat gca acg gtg tcg tgg tac cgc aca aat gcc gat gcc   1008
Asp Gly Ile Asp Ala Thr Val Ser Trp Tyr Arg Thr Asn Ala Asp Ala
                325                 330                 335

gtg agg agg taa                                                  1020
Val Arg Arg
```

<210> 16
<211> 339
<212> PRT
<213> Mycobacterium

<400> 16

```
Val Arg Trp His Thr Met Asp Arg His Ala Asp Val Ala Trp Leu Gly
  1               5                  10                  15

Arg Ser Lys Leu Thr Thr Thr Pro Gly Pro Leu Asp Arg Ala Thr Pro
             20                  25                  30

Val Tyr Ile Ala Gly His Arg Gly Leu Val Gly Ser Ala Leu Val Arg
         35                  40                  45

Arg Phe Glu Ala Glu Gly Phe Thr Asn Leu Ile Val Arg Ser Arg Asp
     50                  55                  60

Glu Ile Asp Leu Thr Asp Arg Ala Ala Thr Phe Asp Phe Val Ser Glu
 65                  70                  75                  80

Thr Arg Pro Gln Val Ile Ile Asp Ala Ala Ala Arg Val Gly Gly Ile
                 85                  90                  95

Met Ala Asn Asn Thr Tyr Pro Ala Asp Phe Leu Ser Glu Asn Leu Arg
            100                 105                 110

Ile Gln Thr Asn Leu Leu Asp Ala Ala Val Ala Val Arg Val Pro Arg
        115                 120                 125

Leu Leu Phe Leu Gly Ser Ser Cys Ile Tyr Pro Lys Tyr Ala Pro Gln
    130                 135                 140

Pro Ile His Glu Ser Ala Leu Leu Thr Gly Pro Leu Glu Pro Thr Asn
145                 150                 155                 160

Asp Ala Tyr Ala Ile Ala Lys Ile Ala Gly Ile Leu Gln Val Gln Ala
                165                 170                 175

Val Arg Arg Gln Tyr Gly Leu Ala Trp Ile Ser Ala Met Pro Thr Asn
            180                 185                 190

Leu Tyr Gly Pro Gly Asp Asn Phe Ser Pro Ser Gly Ser His Leu Leu
        195                 200                 205
```

Pro Ala Leu Ile Arg Arg Tyr Glu Glu Ala Lys Ala Gly Gly Ala Glu
210 215 220

Glu Val Thr Asn Trp Gly Thr Gly Thr Pro Arg Arg Glu Leu Leu His
225 230 235 240

Val Asp Asp Leu Ala Ser Ala Cys Leu Phe Leu Leu Glu His Phe Asp
245 250 255

Gly Pro Asn His Val Asn Val Gly Thr Gly Val Asp His Ser Ile Ser
260 265 270

Glu Ile Ala Asp Met Val Ala Thr Ala Val Gly Tyr Ile Gly Glu Thr
275 280 285

Arg Trp Asp Pro Thr Lys Pro Asp Gly Thr Pro Arg Lys Leu Leu Asp
290 295 300

Val Ser Ala Leu Arg Glu Leu Gly Trp Arg Pro Arg Ile Ala Leu Lys
305 310 315 320

Asp Gly Ile Asp Ala Thr Val Ser Trp Tyr Arg Thr Asn Ala Asp Ala
325 330 335

Val Arg Arg

<210> 17
<211> 723
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(720)

<400> 17
atg gat ttt ttg cgc aac gcc ggc ttg atg gct cgt aac gtt agt acc 48
Met Asp Phe Leu Arg Asn Ala Gly Leu Met Ala Arg Asn Val Ser Thr
1 5 10 15

gag atg ctg cgc cac ttc gaa cga aag cgc cta tta gta aac caa ttc 96
Glu Met Leu Arg His Phe Glu Arg Lys Arg Leu Leu Val Asn Gln Phe
20 25 30

aaa gca tac gga gtc aac gtt gtt att gat gtc ggt gct aac tcc ggc 144
Lys Ala Tyr Gly Val Asn Val Val Ile Asp Val Gly Ala Asn Ser Gly
35 40 45

cag ttc ggt agc gct ttg cgt cgt gca gga ttc aag agc cgt atc gtt 192
Gln Phe Gly Ser Ala Leu Arg Arg Ala Gly Phe Lys Ser Arg Ile Val
50 55 60

tcc ttt gaa cct ctt tcg ggg cca ttt gcg caa cta acg cgc aag tcg 240
Ser Phe Glu Pro Leu Ser Gly Pro Phe Ala Gln Leu Thr Arg Lys Ser
65 70 75 80

gca tcg gat cca cta tgg gag tgt cac cag tat gcc cta ggc gac gcc 288
Ala Ser Asp Pro Leu Trp Glu Cys His Gln Tyr Ala Leu Gly Asp Ala
85 90 95

```
gat gag acg att acc atc aat gtg gca ggc aat gcg ggg gca agt agt   336
Asp Glu Thr Ile Thr Ile Asn Val Ala Gly Asn Ala Gly Ala Ser Ser
            100                 105                 110

tcc gtg ctg ccg atg ctt aaa agt cat caa gat gcc ttt cct ccc gcg   384
Ser Val Leu Pro Met Leu Lys Ser His Gln Asp Ala Phe Pro Pro Ala
        115                 120                 125

aat tat att ggc acc gaa gac gtt gca ata cac cgc ctt gat tcg gtt   432
Asn Tyr Ile Gly Thr Glu Asp Val Ala Ile His Arg Leu Asp Ser Val
    130                 135                 140

gca tca gaa ttt ctg aac cct acc gat gtt act ttc ctg aag atc gac   480
Ala Ser Glu Phe Leu Asn Pro Thr Asp Val Thr Phe Leu Lys Ile Asp
145                 150                 155                 160

gta cag ggt ttc gag aag cag gtt atc acg ggc agt aag tca acg ctt   528
Val Gln Gly Phe Glu Lys Gln Val Ile Thr Gly Ser Lys Ser Thr Leu
                165                 170                 175

aac gaa agc tgc gtc ggc atg caa ctc gaa ctt tct ttt att ccg ttg   576
Asn Glu Ser Cys Val Gly Met Gln Leu Glu Leu Ser Phe Ile Pro Leu
            180                 185                 190

tac gaa ggt gac atg ctg att cat gaa gcg ctt gaa ctt gtc tat tcc   624
Tyr Glu Gly Asp Met Leu Ile His Glu Ala Leu Glu Leu Val Tyr Ser
        195                 200                 205

cta ggt ttc aga ctg acg ggt ttg ttg ccc ggc ttt acg gat ccg cgc   672
Leu Gly Phe Arg Leu Thr Gly Leu Leu Pro Gly Phe Thr Asp Pro Arg
    210                 215                 220

aat ggt cga atg ctt caa gct gac ggc att ttc ttc cgt ggg gac gat   720
Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg Gly Asp Asp
225                 230                 235                 240

tga                                                               723
```

<210> 18
<211> 240
<212> PRT
<213> Mycobacterium

<400> 18

```
Met Asp Phe Leu Arg Asn Ala Gly Leu Met Ala Arg Asn Val Ser Thr
  1               5                  10                  15

Glu Met Leu Arg His Phe Glu Arg Lys Arg Leu Leu Val Asn Gln Phe
             20                  25                  30

Lys Ala Tyr Gly Val Asn Val Val Ile Asp Val Gly Ala Asn Ser Gly
         35                  40                  45

Gln Phe Gly Ser Ala Leu Arg Arg Ala Gly Phe Lys Ser Arg Ile Val
     50                  55                  60

Ser Phe Glu Pro Leu Ser Gly Pro Phe Ala Gln Leu Thr Arg Lys Ser
 65                  70                  75                  80
```

```
Ala Ser Asp Pro Leu Trp Glu Cys His Gln Tyr Ala Leu Gly Asp Ala
                 85                  90                  95

Asp Glu Thr Ile Thr Ile Asn Val Ala Gly Asn Ala Gly Ala Ser Ser
            100                 105                 110

Ser Val Leu Pro Met Leu Lys Ser His Gln Asp Ala Phe Pro Pro Ala
        115                 120                 125

Asn Tyr Ile Gly Thr Glu Asp Val Ala Ile His Arg Leu Asp Ser Val
    130                 135                 140

Ala Ser Glu Phe Leu Asn Pro Thr Asp Val Thr Phe Leu Lys Ile Asp
145                 150                 155                 160

Val Gln Gly Phe Glu Lys Gln Val Ile Thr Gly Ser Lys Ser Thr Leu
                165                 170                 175

Asn Glu Ser Cys Val Gly Met Gln Leu Glu Leu Ser Phe Ile Pro Leu
            180                 185                 190

Tyr Glu Gly Asp Met Leu Ile His Glu Ala Leu Glu Leu Val Tyr Ser
        195                 200                 205

Leu Gly Phe Arg Leu Thr Gly Leu Leu Pro Gly Phe Thr Asp Pro Arg
    210                 215                 220

Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg Gly Asp Asp
225                 230                 235                 240
```

<210> 19
<211> 723
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(720)

<400> 19

```
atg gat ttt ttg cgc aac gcc ggc ttg atg gct cgt aac gtt agc acc   48
Met Asp Phe Leu Arg Asn Ala Gly Leu Met Ala Arg Asn Val Ser Thr
  1               5                  10                  15

gag atg ctg cgc cac ttc gaa cga aag cgc cta tta gta aac caa ttc   96
Glu Met Leu Arg His Phe Glu Arg Lys Arg Leu Leu Val Asn Gln Phe
            20                  25                  30

aaa gca tac gga gtc aac gtt gtt att gat gtc ggt gct aac tcc ggc   144
Lys Ala Tyr Gly Val Asn Val Val Ile Asp Val Gly Ala Asn Ser Gly
        35                  40                  45

cag ttc ggt agc gct ttg cgt cgt gca gga ttc aag agc cgt atc gtt   192
Gln Phe Gly Ser Ala Leu Arg Arg Ala Gly Phe Lys Ser Arg Ile Val
    50                  55                  60

tcc ttt gaa cct ctt tcg ggg cca ttt gcg caa cta acg cgc gag tcg   240
Ser Phe Glu Pro Leu Ser Gly Pro Phe Ala Gln Leu Thr Arg Glu Ser
65                  70                  75                  80
```

```
gca tcg gat cca cta tgg gag tgt cac cag tat gcc cta ggc gac gcc   288
Ala Ser Asp Pro Leu Trp Glu Cys His Gln Tyr Ala Leu Gly Asp Ala
                 85                  90                  95

gat gag acg att acc atc aat gtg gca ggc aat gcg ggg gca agt agt   336
Asp Glu Thr Ile Thr Ile Asn Val Ala Gly Asn Ala Gly Ala Ser Ser
            100                 105                 110

tcc gtg ctg ccg atg ctt aaa agt cat caa gat gcc ttt cct ccc gcg   384
Ser Val Leu Pro Met Leu Lys Ser His Gln Asp Ala Phe Pro Pro Ala
        115                 120                 125

aat tat att ggc acc gaa gac gtt gca ata cac cgc ctt gat tcg gtt   432
Asn Tyr Ile Gly Thr Glu Asp Val Ala Ile His Arg Leu Asp Ser Val
    130                 135                 140

gca tca gaa ttt ctg aac cct acc gat gtt act ttc ctg aag atc gac   480
Ala Ser Glu Phe Leu Asn Pro Thr Asp Val Thr Phe Leu Lys Ile Asp
145                 150                 155                 160

gta cag ggt ttc gag aag cag gtt atc gcg ggc agt aag tca acg ctt   528
Val Gln Gly Phe Glu Lys Gln Val Ile Ala Gly Ser Lys Ser Thr Leu
                165                 170                 175

aac gaa agc tgc gtc ggc atg caa ctc gaa ctt tct ttt att ccg ttg   576
Asn Glu Ser Cys Val Gly Met Gln Leu Glu Leu Ser Phe Ile Pro Leu
            180                 185                 190

tac gaa ggt gac atg ctg att cat gaa gcg ctt gaa ctt gtc tat tcc   624
Tyr Glu Gly Asp Met Leu Ile His Glu Ala Leu Glu Leu Val Tyr Ser
        195                 200                 205

cta ggt ttc aga ctg acg ggt ttg ttg ccc gga ttt acg gat ccg cgc   672
Leu Gly Phe Arg Leu Thr Gly Leu Leu Pro Gly Phe Thr Asp Pro Arg
    210                 215                 220

aat ggt cga atg ctt caa gct gac ggc att ttc ttc cgt ggg gac gat   720
Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg Gly Asp Asp
225                 230                 235                 240

tga                                                               723
```

<210> 20
<211> 240
<212> PRT
<213> Mycobacterium

<400> 20

```
Met Asp Phe Leu Arg Asn Ala Gly Leu Met Ala Arg Asn Val Ser Thr
  1               5                  10                  15

Glu Met Leu Arg His Phe Glu Arg Lys Arg Leu Leu Val Asn Gln Phe
             20                  25                  30

Lys Ala Tyr Gly Val Asn Val Val Ile Asp Val Gly Ala Asn Ser Gly
         35                  40                  45

Gln Phe Gly Ser Ala Leu Arg Arg Ala Gly Phe Lys Ser Arg Ile Val
     50                  55                  60
```

```
Ser Phe Glu Pro Leu Ser Gly Pro Phe Ala Gln Leu Thr Arg Glu Ser
 65                  70                  75                  80

Ala Ser Asp Pro Leu Trp Glu Cys His Gln Tyr Ala Leu Gly Asp Ala
                85                  90                  95

Asp Glu Thr Ile Thr Ile Asn Val Ala Gly Asn Ala Gly Ala Ser Ser
            100                 105                 110

Ser Val Leu Pro Met Leu Lys Ser His Gln Asp Ala Phe Pro Pro Ala
        115                 120                 125

Asn Tyr Ile Gly Thr Glu Asp Val Ala Ile His Arg Leu Asp Ser Val
    130                 135                 140

Ala Ser Glu Phe Leu Asn Pro Thr Asp Val Thr Phe Leu Lys Ile Asp
145                 150                 155                 160

Val Gln Gly Phe Glu Lys Gln Val Ile Ala Gly Ser Lys Ser Thr Leu
                165                 170                 175

Asn Glu Ser Cys Val Gly Met Gln Leu Glu Leu Ser Phe Ile Pro Leu
            180                 185                 190

Tyr Glu Gly Asp Met Leu Ile His Glu Ala Leu Glu Leu Val Tyr Ser
        195                 200                 205

Leu Gly Phe Arg Leu Thr Gly Leu Leu Pro Gly Phe Thr Asp Pro Arg
    210                 215                 220

Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg Gly Asp Asp
225                 230                 235                 240


<210> 21
<211> 801
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(798)

<400> 21
atg act gcg cca gtg ttc tcg ata att atc cct acc ttc aat gca gcg   48
Met Thr Ala Pro Val Phe Ser Ile Ile Ile Pro Thr Phe Asn Ala Ala
  1               5                  10                  15

gtg acg ctg caa gcc tgc ctc gga agc atc gtc ggg cag acc tac cgg   96
Val Thr Leu Gln Ala Cys Leu Gly Ser Ile Val Gly Gln Thr Tyr Arg
             20                  25                  30

gaa gtg gaa gtg gtc ctt gtc gac ggc ggt tcg acc gat cgg acc ctc   144
Glu Val Glu Val Val Leu Val Asp Gly Gly Ser Thr Asp Arg Thr Leu
         35                  40                  45

gac atc gcg aac agt ttc cgc ccg gaa ctc ggc tcg cga ctg gtc gtt   192
Asp Ile Ala Asn Ser Phe Arg Pro Glu Leu Gly Ser Arg Leu Val Val
     50                  55                  60
```

```
cac agc ggg ccc gat gat ggc ccc tac gac gcc atg aac cgc ggc gtc   240
His Ser Gly Pro Asp Asp Gly Pro Tyr Asp Ala Met Asn Arg Gly Val
 65                  70                  75                  80

ggc gtg gcc aca ggc gaa tgg gta ctt ttt tta ggc gcc gac gac acc   288
Gly Val Ala Thr Gly Glu Trp Val Leu Phe Leu Gly Ala Asp Asp Thr
                 85                  90                  95

ctc tac gaa cca acc acg ttg gcc cag gta gcc gct ttt ctc ggc gac   336
Leu Tyr Glu Pro Thr Thr Leu Ala Gln Val Ala Ala Phe Leu Gly Asp
            100                 105                 110

cat gcg gca agc cat ctt gtc tat ggc gat gtt gtg atg cgt tcg acg   384
His Ala Ala Ser His Leu Val Tyr Gly Asp Val Val Met Arg Ser Thr
        115                 120                 125

aaa agc cgg cat gcc gga cct ttc gac ctc gac cgc ctc cta ttt gag   432
Lys Ser Arg His Ala Gly Pro Phe Asp Leu Asp Arg Leu Leu Phe Glu
    130                 135                 140

acg aat ttg tgc cac caa tcg atc ttt tac cgc cgt gag ctt ttc gac   480
Thr Asn Leu Cys His Gln Ser Ile Phe Tyr Arg Arg Glu Leu Phe Asp
145                 150                 155                 160

ggc atc ggc cct tac aac ctg cgc tac cga gtc tgg gcg gac tgg gac   528
Gly Ile Gly Pro Tyr Asn Leu Arg Tyr Arg Val Trp Ala Asp Trp Asp
                165                 170                 175

ttc aat att cgc tgc ttc tcc aac ccg gcg ctg att acc cgc tac atg   576
Phe Asn Ile Arg Cys Phe Ser Asn Pro Ala Leu Ile Thr Arg Tyr Met
            180                 185                 190

gac gtc gtg att tcc gaa tac aac gac atg acc ggc ttc agc atg agg   624
Asp Val Val Ile Ser Glu Tyr Asn Asp Met Thr Gly Phe Ser Met Arg
        195                 200                 205

cag ggg act gat aaa gag ttc aga aaa cgg ctg cca atg tac ttc tgg   672
Gln Gly Thr Asp Lys Glu Phe Arg Lys Arg Leu Pro Met Tyr Phe Trp
    210                 215                 220

gtt gca ggg tgg gag act tgc agg cgc atg ctg gcg ttt ttg aaa gac   720
Val Ala Gly Trp Glu Thr Cys Arg Arg Met Leu Ala Phe Leu Lys Asp
225                 230                 235                 240

aag gag aat cgc cgt ctg gcc ttg cgt acg cgg ttg ata agg gtt aag   768
Lys Glu Asn Arg Arg Leu Ala Leu Arg Thr Arg Leu Ile Arg Val Lys
                245                 250                 255

gcc gtc tcc aaa gaa cga agc gca gaa ccg tag                      801
Ala Val Ser Lys Glu Arg Ser Ala Glu Pro
            260                 265


<210> 22
<211> 266
<212> PRT
<213> Mycobacterium

<400> 22
Met Thr Ala Pro Val Phe Ser Ile Ile Ile Pro Thr Phe Asn Ala Ala
  1               5                  10                  15
```

```
Val Thr Leu Gln Ala Cys Leu Gly Ser Ile Val Gly Gln Thr Tyr Arg
            20                  25                  30

Glu Val Glu Val Val Leu Val Asp Gly Gly Ser Thr Asp Arg Thr Leu
        35                  40                  45

Asp Ile Ala Asn Ser Phe Arg Pro Glu Leu Gly Ser Arg Leu Val Val
    50                  55                  60

His Ser Gly Pro Asp Asp Gly Pro Tyr Asp Ala Met Asn Arg Gly Val
65                  70                  75                  80

Gly Val Ala Thr Gly Glu Trp Val Leu Phe Leu Gly Ala Asp Asp Thr
                85                  90                  95

Leu Tyr Glu Pro Thr Thr Leu Ala Gln Val Ala Ala Phe Leu Gly Asp
            100                 105                 110

His Ala Ala Ser His Leu Val Tyr Gly Asp Val Val Met Arg Ser Thr
        115                 120                 125

Lys Ser Arg His Ala Gly Pro Phe Asp Leu Asp Arg Leu Leu Phe Glu
    130                 135                 140

Thr Asn Leu Cys His Gln Ser Ile Phe Tyr Arg Arg Glu Leu Phe Asp
145                 150                 155                 160

Gly Ile Gly Pro Tyr Asn Leu Arg Tyr Arg Val Trp Ala Asp Trp Asp
                165                 170                 175

Phe Asn Ile Arg Cys Phe Ser Asn Pro Ala Leu Ile Thr Arg Tyr Met
            180                 185                 190

Asp Val Val Ile Ser Glu Tyr Asn Asp Met Thr Gly Phe Ser Met Arg
        195                 200                 205

Gln Gly Thr Asp Lys Glu Phe Arg Lys Arg Leu Pro Met Tyr Phe Trp
    210                 215                 220

Val Ala Gly Trp Glu Thr Cys Arg Arg Met Leu Ala Phe Leu Lys Asp
225                 230                 235                 240

Lys Glu Asn Arg Arg Leu Ala Leu Arg Thr Arg Leu Ile Arg Val Lys
                245                 250                 255

Ala Val Ser Lys Glu Arg Ser Ala Glu Pro
            260                 265
```

<210> 23
<211> 801
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(798)

<400> 23

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atg act gcg cca gtg ttc tcg ata att atc cct acc ttc aat gca gcg   48
Met Thr Ala Pro Val Phe Ser Ile Ile Ile Pro Thr Phe Asn Ala Ala
  1               5                  10                  15

gtg acg ctg caa gcc tgc ctc gga agc atc gtc ggg cag acc tac cgg   96
Val Thr Leu Gln Ala Cys Leu Gly Ser Ile Val Gly Gln Thr Tyr Arg
             20                  25                  30

gaa gtg gaa gtg gtc ctt gtc gac ggc ggt tcg acc gat cgg acc ctc   144
Glu Val Glu Val Val Leu Val Asp Gly Gly Ser Thr Asp Arg Thr Leu
         35                  40                  45

gac atc gcg aac agt ttc cgc ccg gaa ctc ggc tcg cga ctg gtc gtt   192
Asp Ile Ala Asn Ser Phe Arg Pro Glu Leu Gly Ser Arg Leu Val Val
     50                  55                  60

cac agc ggg ccc gat gat ggc ccc tac gac gcc atg aac cgc ggc gtc   240
His Ser Gly Pro Asp Asp Gly Pro Tyr Asp Ala Met Asn Arg Gly Val
 65                  70                  75                  80

ggc gta gcc aca ggc gaa tgg gta ctt ttt tta ggc gcc gac gac acc   288
Gly Val Ala Thr Gly Glu Trp Val Leu Phe Leu Gly Ala Asp Asp Thr
                 85                  90                  95

ctc tac gaa cca acc acg ttg gcc cag gta gcc gct ttt ctc ggc gac   336
Leu Tyr Glu Pro Thr Thr Leu Ala Gln Val Ala Ala Phe Leu Gly Asp
            100                 105                 110

cat gcg gca agc cat ctt gtc tat ggc gat gtt gtg atg cgt tcg acg   384
His Ala Ala Ser His Leu Val Tyr Gly Asp Val Val Met Arg Ser Thr
        115                 120                 125

aaa agc cgg cat gcc gga cct ttc gac ctc gac cgc ctc cta ttt gag   432
Lys Ser Arg His Ala Gly Pro Phe Asp Leu Asp Arg Leu Leu Phe Glu
    130                 135                 140

acg aat ttg tgc cac caa tcg atc ttt tac cgc cgt gag ctt ttc gac   480
Thr Asn Leu Cys His Gln Ser Ile Phe Tyr Arg Arg Glu Leu Phe Asp
145                 150                 155                 160

ggc atc ggc cct tac aac ctg cgc tac cga gtc tgg gcg gac tgg gac   528
Gly Ile Gly Pro Tyr Asn Leu Arg Tyr Arg Val Trp Ala Asp Trp Asp
                165                 170                 175

ttc aat att cgc tgc ttc tcc aac ccg gcg ctg att acc cgc tac atg   576
Phe Asn Ile Arg Cys Phe Ser Asn Pro Ala Leu Ile Thr Arg Tyr Met
            180                 185                 190

gac gtc gtg att tcc gaa tac aac gac atg acc ggc ttc agc atg agg   624
Asp Val Val Ile Ser Glu Tyr Asn Asp Met Thr Gly Phe Ser Met Arg
        195                 200                 205

cag ggg act gat aaa gag ttc aga aaa cgg ctg cca atg tac ttc tgg   672
Gln Gly Thr Asp Lys Glu Phe Arg Lys Arg Leu Pro Met Tyr Phe Trp
    210                 215                 220

gtt gca ggg tgg gag act tgc agg cgc atg ctg gcg ttt ttg aaa gac   720
Val Ala Gly Trp Glu Thr Cys Arg Arg Met Leu Ala Phe Leu Lys Asp
225                 230                 235                 240
```

```
aag gag aat cgc cgt ctg gcc ttg cgt acg cgg ttg ata agg gtt aag   768
Lys Glu Asn Arg Arg Leu Ala Leu Arg Thr Arg Leu Ile Arg Val Lys
                245                 250                 255

gcc gtc tcc aaa gaa cga agc gca gaa ccg tag                      801
Ala Val Ser Lys Glu Arg Ser Ala Glu Pro
            260                 265
```

<210> 24
<211> 266
<212> PRT
<213> Mycobacterium

<400> 24

```
Met Thr Ala Pro Val Phe Ser Ile Ile Ile Pro Thr Phe Asn Ala Ala
  1               5                  10                  15

Val Thr Leu Gln Ala Cys Leu Gly Ser Ile Val Gly Gln Thr Tyr Arg
             20                  25                  30

Glu Val Glu Val Val Leu Val Asp Gly Gly Ser Thr Asp Arg Thr Leu
         35                  40                  45

Asp Ile Ala Asn Ser Phe Arg Pro Glu Leu Gly Ser Arg Leu Val Val
     50                  55                  60

His Ser Gly Pro Asp Asp Gly Pro Tyr Asp Ala Met Asn Arg Gly Val
 65                  70                  75                  80

Gly Val Ala Thr Gly Glu Trp Val Leu Phe Leu Gly Ala Asp Asp Thr
                 85                  90                  95

Leu Tyr Glu Pro Thr Thr Leu Ala Gln Val Ala Ala Phe Leu Gly Asp
            100                 105                 110

His Ala Ala Ser His Leu Val Tyr Gly Asp Val Val Met Arg Ser Thr
        115                 120                 125

Lys Ser Arg His Ala Gly Pro Phe Asp Leu Asp Arg Leu Leu Phe Glu
    130                 135                 140

Thr Asn Leu Cys His Gln Ser Ile Phe Tyr Arg Arg Glu Leu Phe Asp
145                 150                 155                 160

Gly Ile Gly Pro Tyr Asn Leu Arg Tyr Arg Val Trp Ala Asp Trp Asp
                165                 170                 175

Phe Asn Ile Arg Cys Phe Ser Asn Pro Ala Leu Ile Thr Arg Tyr Met
            180                 185                 190

Asp Val Val Ile Ser Glu Tyr Asn Asp Met Thr Gly Phe Ser Met Arg
        195                 200                 205

Gln Gly Thr Asp Lys Glu Phe Arg Lys Arg Leu Pro Met Tyr Phe Trp
    210                 215                 220

Val Ala Gly Trp Glu Thr Cys Arg Arg Met Leu Ala Phe Leu Lys Asp
225                 230                 235                 240
```

```
Lys Glu Asn Arg Arg Leu Ala Leu Arg Thr Arg Leu Ile Arg Val Lys
                245                 250                 255

Ala Val Ser Lys Glu Arg Ser Ala Glu Pro
            260                 265
```

<210> 25
<211> 867
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(864)

<400> 25

```
gtg gcc agc aga agt ccc cac tcc gct gcg ggt ggt tgg cta att ctt   48
Val Ala Ser Arg Ser Pro His Ser Ala Ala Gly Gly Trp Leu Ile Leu
  1               5                  10                  15

ggc ggc tcc ctt ctt gtg gtc ggc gtg gcg cat ccg gta gga ctc gcc   96
Gly Gly Ser Leu Leu Val Val Gly Val Ala His Pro Val Gly Leu Ala
             20                  25                  30

gga ggt gac gac gat gct ggc gtg gtg cag cag ccg atc gag gat gct   144
Gly Gly Asp Asp Asp Ala Gly Val Val Gln Gln Pro Ile Glu Asp Ala
         35                  40                  45

ggc ggc ggt ggt gtg ctc ggg cag gaa tcg ccc cca ttg ttc gaa ggg   192
Gly Gly Gly Gly Val Leu Gly Gln Glu Ser Pro Pro Leu Phe Glu Gly
     50                  55                  60

cca atg cga ggc gat ggc cag gga gcg gcg ctc gta gcc ggc agc cac   240
Pro Met Arg Gly Asp Gly Gln Gly Ala Ala Leu Val Ala Gly Ser His
 65                  70                  75                  80

gag ccg gaa caa cag ttg agt ccc ggt gtc gtc gag cgg ggc gaa gcc   288
Glu Pro Glu Gln Gln Leu Ser Pro Gly Val Val Glu Arg Gly Glu Ala
                 85                  90                  95

gat ctc gtc caa gat gac cag atc cgc gcg gag cag ggt gtc gat gat   336
Asp Leu Val Gln Asp Asp Gln Ile Arg Ala Glu Gln Gly Val Asp Asp
            100                 105                 110

ctt gcc gac ggt gtt gtc ggc cag gcc gcg gta gag gac ctc gat cag   384
Leu Ala Asp Gly Val Val Gly Gln Ala Ala Val Glu Asp Leu Asp Gln
        115                 120                 125

gtc ggc ggc ggt gaa gta gcg gac ttt gaa tcc ggc gtg gac ggc agc   432
Val Gly Gly Gly Glu Val Ala Asp Phe Glu Ser Gly Val Asp Gly Ser
    130                 135                 140

gtg ccc gca gcc gat gag cag gtg act ttt gcc cgt acc agg tgg gcc   480
Val Pro Ala Ala Asp Glu Gln Val Thr Phe Ala Arg Thr Arg Trp Ala
145                 150                 155                 160

aat gac cgc cag gtt ctg ttg tgc ccg aat cca ttc cag gct cga cag   528
Asn Asp Arg Gln Val Leu Leu Cys Pro Asn Pro Phe Gln Ala Arg Gln
                165                 170                 175
```

```
gta gtc gaa cgt ggc tgc ggt gat cga cga tcc ggt gac gtc gaa ccc   576
Val Val Glu Arg Gly Cys Gly Asp Arg Arg Ser Gly Asp Val Glu Pro
            180                 185                 190

gtc gag ggt ctt ggt gac cgg gaa ggc tgc ggc ctt gag acg gtt ggc   624
Val Glu Gly Leu Gly Asp Arg Glu Gly Cys Gly Leu Glu Thr Val Gly
        195                 200                 205

ggt gtt gga ggc atc gcg ggc agc gat ctc ggc ctc aac caa cgt ccg   672
Gly Val Gly Gly Ile Ala Gly Ser Asp Leu Gly Leu Asn Gln Arg Pro
    210                 215                 220

cag gat ctc ctc cgg tgt cca gcg ttg cgt ctt ggc gac ttg caa cac   720
Gln Asp Leu Leu Arg Cys Pro Ala Leu Arg Leu Gly Asp Leu Gln His
225                 230                 235                 240

ctc ggc ggc gtt gcg gcg cac cgt ggc cag ctt caa ccg ccg cag cgc   768
Leu Gly Gly Val Ala Ala His Arg Gly Gln Leu Gln Pro Pro Gln Arg
                245                 250                 255

cgc gtc aag gtc agc agc cag cgg tgc cgc cga gga cgg tgc cac cgg   816
Arg Val Lys Val Ser Ser Gln Arg Cys Arg Arg Gly Arg Cys His Arg
            260                 265                 270

ctt ggc agc ggt ggt cat gag gcc gtc ccg tcg gtg gtg ttg atc ttg   864
Leu Gly Ser Gly Gly His Glu Ala Val Pro Ser Val Val Leu Ile Leu
        275                 280                 285

tag                                                               867
```

<210> 26
<211> 288
<212> PRT
<213> Mycobacterium

<400> 26

```
Val Ala Ser Arg Ser Pro His Ser Ala Ala Gly Gly Trp Leu Ile Leu
  1               5                  10                  15

Gly Gly Ser Leu Leu Val Val Gly Val Ala His Pro Val Gly Leu Ala
            20                  25                  30

Gly Gly Asp Asp Asp Ala Gly Val Val Gln Gln Pro Ile Glu Asp Ala
        35                  40                  45

Gly Gly Gly Gly Val Leu Gly Gln Glu Ser Pro Pro Leu Phe Glu Gly
    50                  55                  60

Pro Met Arg Gly Asp Gly Gln Gly Ala Ala Leu Val Ala Gly Ser His
65                  70                  75                  80

Glu Pro Glu Gln Gln Leu Ser Pro Gly Val Val Glu Arg Gly Glu Ala
                85                  90                  95

Asp Leu Val Gln Asp Asp Gln Ile Arg Ala Glu Gln Gly Val Asp Asp
            100                 105                 110

Leu Ala Asp Gly Val Val Gly Gln Ala Ala Val Glu Asp Leu Asp Gln
        115                 120                 125
```

```
Val Gly Gly Gly Glu Val Ala Asp Phe Glu Ser Gly Val Asp Gly Ser
    130                 135                 140

Val Pro Ala Ala Asp Glu Gln Val Thr Phe Ala Arg Thr Arg Trp Ala
145                 150                 155                 160

Asn Asp Arg Gln Val Leu Leu Cys Pro Asn Pro Phe Gln Ala Arg Gln
                165                 170                 175

Val Val Glu Arg Gly Cys Gly Asp Arg Arg Ser Gly Asp Val Glu Pro
            180                 185                 190

Val Glu Gly Leu Gly Asp Arg Glu Gly Cys Gly Leu Glu Thr Val Gly
        195                 200                 205

Gly Val Gly Gly Ile Ala Gly Ser Asp Leu Gly Leu Asn Gln Arg Pro
    210                 215                 220

Gln Asp Leu Leu Arg Cys Pro Ala Leu Arg Leu Gly Asp Leu Gln His
225                 230                 235                 240

Leu Gly Gly Val Ala Ala His Arg Gly Gln Leu Gln Pro Pro Gln Arg
                245                 250                 255

Arg Val Lys Val Ser Ser Gln Arg Cys Arg Arg Gly Arg Cys His Arg
            260                 265                 270

Leu Gly Ser Gly Gly His Glu Ala Val Pro Ser Val Val Leu Ile Leu
        275                 280                 285


<210> 27
<211> 1739
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(945)

<400> 27
atg ggc tgc ctc aaa ggt ggt gtc gtc gcc aat gtt gtt gtt cca aca   48
Met Gly Cys Leu Lys Gly Gly Val Val Ala Asn Val Val Val Pro Thr
  1               5                  10                  15

ccg gat tat gtg cga ttc gcg tcc cac tat ggc ttc gtt ccg gac ttc   96
Pro Asp Tyr Val Arg Phe Ala Ser His Tyr Gly Phe Val Pro Asp Phe
             20                  25                  30

tgc cac ggt gcg gat ccg caa tcg aag ggc atc gtg gag aac ctc tgt   144
Cys His Gly Ala Asp Pro Gln Ser Lys Gly Ile Val Glu Asn Leu Cys
         35                  40                  45

ggc tac gct cag gac gac ctt gcg gtg ccg ctg ctg acc gaa gct gcg   192
Gly Tyr Ala Gln Asp Asp Leu Ala Val Pro Leu Leu Thr Glu Ala Ala
     50                  55                  60

tta gcc ggt gag cag gtc gac cta cgt gcc ctc aac gcc cag gcg caa   240
Leu Ala Gly Glu Gln Val Asp Leu Arg Ala Leu Asn Ala Gln Ala Gln
 65                  70                  75                  80
```

```
cta tgg tgc gcc gag gtc aat gcc acg gtc cac tcg gag atc tgc gcc   288
Leu Trp Cys Ala Glu Val Asn Ala Thr Val His Ser Glu Ile Cys Ala
                 85                  90                  95

gtg ccc aac gat cgc ttg gtt gac gag cgc acc gtc ttg agg gag ctg   336
Val Pro Asn Asp Arg Leu Val Asp Glu Arg Thr Val Leu Arg Glu Leu
            100                 105                 110

ccc tcg ctg cgg ccg acg atc ggc tcg ggg tcg gtg cgc cgt aag gtc   384
Pro Ser Leu Arg Pro Thr Ile Gly Ser Gly Ser Val Arg Arg Lys Val
        115                 120                 125

gac ggc ctc tcg tgc atc cgt tac ggc tca gct cgt tac tcg gtg cct   432
Asp Gly Leu Ser Cys Ile Arg Tyr Gly Ser Ala Arg Tyr Ser Val Pro
    130                 135                 140

cag cgg ctc gtc ggt gcc acc gtg gcg gtg gtg gtc gat cat ggc gcc   480
Gln Arg Leu Val Gly Ala Thr Val Ala Val Val Val Asp His Gly Ala
145                 150                 155                 160

ctg atc ctg ttg gaa cct gcg acc ggt gtg atc gtg gcc gag cac gag   528
Leu Ile Leu Leu Glu Pro Ala Thr Gly Val Ile Val Ala Glu His Glu
                165                 170                 175

ctc gtc agc cca ggt gag gtg tcc atc ctc gat gaa cac tac gac gga   576
Leu Val Ser Pro Gly Glu Val Ser Ile Leu Asp Glu His Tyr Asp Gly
            180                 185                 190

ccc aga ccc gca ccc tcg cgt ggt cct cgc ccg aaa acc caa gca gag   624
Pro Arg Pro Ala Pro Ser Arg Gly Pro Arg Pro Lys Thr Gln Ala Glu
        195                 200                 205

aaa cga ttc tgc gca ttg gga acc gaa gcg cag cag ttc ctc gtc ggt   672
Lys Arg Phe Cys Ala Leu Gly Thr Glu Ala Gln Gln Phe Leu Val Gly
    210                 215                 220

gct gct gcg atc ggc aac acc cga ctg aaa tcc gaa ctc gac att ctg   720
Ala Ala Ala Ile Gly Asn Thr Arg Leu Lys Ser Glu Leu Asp Ile Leu
225                 230                 235                 240

ctc ggc ctt ggc gcc gcc cac ggc gaa cag gct ttg att gac gcg ctg   768
Leu Gly Leu Gly Ala Ala His Gly Glu Gln Ala Leu Ile Asp Ala Leu
                245                 250                 255

cgc cgg gcg gtt gcg ttt cgc cgg ttc cgc gct gcc gac gtg cgc tcg   816
Arg Arg Ala Val Ala Phe Arg Arg Phe Arg Ala Ala Asp Val Arg Ser
            260                 265                 270

atc ctg gcc gcc ggc gcc ggc acc cca caa ccc cgc ccc gcc ggc gac   864
Ile Leu Ala Ala Gly Ala Gly Thr Pro Gln Pro Arg Pro Ala Gly Asp
        275                 280                 285

gca ctc gtg ctc gat ctg ccc acc gtc gag acc cgc tcg ttg gag gcc   912
Ala Leu Val Leu Asp Leu Pro Thr Val Glu Thr Arg Ser Leu Glu Ala
    290                 295                 300

tac aag atc aac acc acc gac ggg acg gcc tca tgaccaccgc tgccaagccg 965
Tyr Lys Ile Asn Thr Thr Asp Gly Thr Ala Ser
305                 310                 315

gtggcaccgt cctcggcggc accgctggct gctgaccttg acgcggcgct gcggcggttg 1025
```

aagctggcca cggtgcgccg caacgccgcc gaggtgttgc aagtcgccaa gacgcaacgc 1085

tggacaccgg aggagatcct gcggacgttg gttgaggccg agatcgctgc ccgcgatgcc 1145

tccaacaccg ccaaccgtct caaggccgca gccttcccgg tcaccaagac cctcgacggg 1205

ttcgacgtca ccggatcgtc gatcaccgca gccacgttcg actacctgtc gagcctggaa 1265

tggattcggg cacaacagaa cctggcggtc attggcccac ctggtacggg caaaagtcac 1325

ctgctcatcg gctgcgggca cgctgccgtc cacgccggat tcaaagtccg ctacttcacc 1385

gccgccgacc tgatcgaggt cctctaccgc ggcctggccg acaacaccgt cggcaagatc 1445

atcgacaccc tgctccgcgc ggatctggtc atcttggacg agatcggctt cgccccgctc 1505

gacgacaccg ggactcaact gttgttccgg ctcgtggctg ccggctacga gcgccgctcc 1565

ctggccatcg cctcgcattg gcccttcgaa caatgggggc gattcctgcc cgagcacacc 1625

accgccgcca gcatcctcga tcggctgctg caccacgcca gcatcgtcgt cacctccggc 1685

gagtcctacc ggatgcgcca cgccgaccac aagaagggag ccgccaagaa ttag 1739

<210> 28
<211> 315
<212> PRT
<213> Mycobacterium

<400> 28

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Met Gly Cys Leu Lys Gly Gly Val Val Ala Asn Val Val Val Pro Thr
  1               5                  10                  15

Pro Asp Tyr Val Arg Phe Ala Ser His Tyr Gly Phe Val Pro Asp Phe
             20                  25                  30

Cys His Gly Ala Asp Pro Gln Ser Lys Gly Ile Val Glu Asn Leu Cys
         35                  40                  45

Gly Tyr Ala Gln Asp Asp Leu Ala Val Pro Leu Leu Thr Glu Ala Ala
     50                  55                  60

Leu Ala Gly Glu Gln Val Asp Leu Arg Ala Leu Asn Ala Gln Ala Gln
 65                  70                  75                  80

Leu Trp Cys Ala Glu Val Asn Ala Thr Val His Ser Glu Ile Cys Ala
                 85                  90                  95

Val Pro Asn Asp Arg Leu Val Asp Glu Arg Thr Val Leu Arg Glu Leu
            100                 105                 110

Pro Ser Leu Arg Pro Thr Ile Gly Ser Gly Ser Val Arg Arg Lys Val
        115                 120                 125

Asp Gly Leu Ser Cys Ile Arg Tyr Gly Ser Ala Arg Tyr Ser Val Pro
    130                 135                 140

Gln Arg Leu Val Gly Ala Thr Val Ala Val Val Val Asp His Gly Ala
145                 150                 155                 160
```

```
Leu Ile Leu Leu Glu Pro Ala Thr Gly Val Ile Val Ala Glu His Glu
                165                 170                 175

Leu Val Ser Pro Gly Glu Val Ser Ile Leu Asp Glu His Tyr Asp Gly
            180                 185                 190

Pro Arg Pro Ala Pro Ser Arg Gly Pro Arg Pro Lys Thr Gln Ala Glu
        195                 200                 205

Lys Arg Phe Cys Ala Leu Gly Thr Glu Ala Gln Gln Phe Leu Val Gly
    210                 215                 220

Ala Ala Ala Ile Gly Asn Thr Arg Leu Lys Ser Glu Leu Asp Ile Leu
225                 230                 235                 240

Leu Gly Leu Gly Ala Ala His Gly Glu Gln Ala Leu Ile Asp Ala Leu
                245                 250                 255

Arg Arg Ala Val Ala Phe Arg Arg Phe Arg Ala Ala Asp Val Arg Ser
            260                 265                 270

Ile Leu Ala Ala Gly Ala Gly Thr Pro Gln Pro Arg Pro Ala Gly Asp
        275                 280                 285

Ala Leu Val Leu Asp Leu Pro Thr Val Glu Thr Arg Ser Leu Glu Ala
    290                 295                 300

Tyr Lys Ile Asn Thr Thr Asp Gly Thr Ala Ser
305                 310                 315


<210> 29
<211> 264
<212> PRT
<213> Mycobacterium

<220>
<221> DOMAIN
<222> (1)..(264)
<223> amino acid sequence is encoded by nucleotides
      945-1736 of SEQ ID NO:27

<400> 29
Met Thr Thr Ala Ala Lys Pro Val Ala Pro Ser Ser Ala Ala Pro Leu
  1               5                  10                  15

Ala Ala Asp Leu Asp Ala Ala Leu Arg Arg Leu Lys Leu Ala Thr Val
             20                  25                  30

Arg Arg Asn Ala Ala Glu Val Leu Gln Val Ala Lys Thr Gln Arg Trp
         35                  40                  45

Thr Pro Glu Glu Ile Leu Arg Thr Leu Val Glu Ala Glu Ile Ala Ala
     50                  55                  60

Arg Asp Ala Ser Asn Thr Ala Asn Arg Leu Lys Ala Ala Ala Phe Pro
 65                  70                  75                  80

Val Thr Lys Thr Leu Asp Gly Phe Asp Val Thr Gly Ser Ser Ile Thr
                 85                  90                  95
```

```
Ala Ala Thr Phe Asp Tyr Leu Ser Ser Leu Glu Trp Ile Arg Ala Gln
            100                 105                 110

Gln Asn Leu Ala Val Ile Gly Pro Pro Gly Thr Gly Lys Ser His Leu
        115                 120                 125

Leu Ile Gly Cys Gly His Ala Ala Val His Ala Gly Phe Lys Val Arg
    130                 135                 140

Tyr Phe Thr Ala Ala Asp Leu Ile Glu Val Leu Tyr Arg Gly Leu Ala
145                 150                 155                 160

Asp Asn Thr Val Gly Lys Ile Ile Asp Thr Leu Leu Arg Ala Asp Leu
                165                 170                 175

Val Ile Leu Asp Glu Ile Gly Phe Ala Pro Leu Asp Asp Thr Gly Thr
            180                 185                 190

Gln Leu Leu Phe Arg Leu Val Ala Ala Gly Tyr Glu Arg Arg Ser Leu
        195                 200                 205

Ala Ile Ala Ser His Trp Pro Phe Glu Gln Trp Gly Arg Phe Leu Pro
    210                 215                 220

Glu His Thr Thr Ala Ala Ser Ile Leu Asp Arg Leu Leu His His Ala
225                 230                 235                 240

Ser Ile Val Val Thr Ser Gly Glu Ser Tyr Arg Met Arg His Ala Asp
                245                 250                 255

His Lys Lys Gly Ala Ala Lys Asn
            260
```

<210> 30
<211> 789
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(786)

<400> 30

```
gtg acg tct gct ccg acc gtc tcg gtg ata acg atc tcg ttc aac gac   48
Met Thr Ser Ala Pro Thr Val Ser Val Ile Thr Ile Ser Phe Asn Asp
  1               5                  10                  15

ctc gac ggg ttg cag cgc acg gtg aaa agt gtg cgg gcg caa cgc tac   96
Leu Asp Gly Leu Gln Arg Thr Val Lys Ser Val Arg Ala Gln Arg Tyr
            20                  25                  30

cgg gga cgc atc gag cac atc gta atc gac ggt ggc agc ggc gac gac  144
Arg Gly Arg Ile Glu His Ile Val Ile Asp Gly Gly Ser Gly Asp Asp
        35                  40                  45

gtg gtg gca tac ctg tcc ggg tgt gaa cca ggc ttc gcg tat tgg cag  192
Val Val Ala Tyr Leu Ser Gly Cys Glu Pro Gly Phe Ala Tyr Trp Gln
    50                  55                  60
```

```
tcc gag ccc gac ggc ggg cgg tac gac gcg atg aac cag ggc atc gcg   240
Ser Glu Pro Asp Gly Gly Arg Tyr Asp Ala Met Asn Gln Gly Ile Ala
 65                  70                  75                  80

cac gca tcg ggt gat ctg ttg tgg ttc ttg cac tcc gcc gat cgt ttt   288
His Ala Ser Gly Asp Leu Leu Trp Phe Leu His Ser Ala Asp Arg Phe
                85                  90                  95

tcc ggg ccc gac gtg gta gcc cag gcc gtg gag gcg cta tcc ggc aag   336
Ser Gly Pro Asp Val Val Ala Gln Ala Val Glu Ala Leu Ser Gly Lys
            100                 105                 110

gga ccg gtg tcc gaa ttg tgg ggc ttc ggg atg gat cgt ctc gtc ggg   384
Gly Pro Val Ser Glu Leu Trp Gly Phe Gly Met Asp Arg Leu Val Gly
        115                 120                 125

ctc gat cgg gtg cgc ggc ccg ata cct ttc agc ctg cgc aaa ttc ctg   432
Leu Asp Arg Val Arg Gly Pro Ile Pro Phe Ser Leu Arg Lys Phe Leu
    130                 135                 140

gcc ggc aag cag gtt gtt ccg cat caa gca tcg ttc ttc gga tca tcg   480
Ala Gly Lys Gln Val Val Pro His Gln Ala Ser Phe Phe Gly Ser Ser
145                 150                 155                 160

ctg gtg gcc aag atc ggt ggc tac gac ctt gat ttc ggg atc gcc gcc   528
Leu Val Ala Lys Ile Gly Gly Tyr Asp Leu Asp Phe Gly Ile Ala Ala
                165                 170                 175

gac cag gaa ttc ata ttg cgg gcc gcg ctg gta tgc gag ccg gtc acg   576
Asp Gln Glu Phe Ile Leu Arg Ala Ala Leu Val Cys Glu Pro Val Thr
            180                 185                 190

att cgg tgt gtg ctg tgc gag ttc gac acc acg ggc gtc ggc tcg cac   624
Ile Arg Cys Val Leu Cys Glu Phe Asp Thr Thr Gly Val Gly Ser His
        195                 200                 205

cgg gaa cca agc gcg gtc ttc ggt gat ctg cgc cgc atg ggc gac ctt   672
Arg Glu Pro Ser Ala Val Phe Gly Asp Leu Arg Arg Met Gly Asp Leu
    210                 215                 220

cat cgc cgc tac ccg ttc ggg gga agg cga ata tca cat gcc tac cta   720
His Arg Arg Tyr Pro Phe Gly Gly Arg Arg Ile Ser His Ala Tyr Leu
225                 230                 235                 240

cgc ggc cgg gag ttc tac gcc tac aac agt cga ttc tgg gaa aac gtc   768
Arg Gly Arg Glu Phe Tyr Ala Tyr Asn Ser Arg Phe Trp Glu Asn Val
                245                 250                 255

ttc acg cga atg tcg aaa tag                                      789
Phe Thr Arg Met Ser Lys
            260
```

<210> 31
<211> 262
<212> PRT
<213> Mycobacterium

<400> 31

```
Met Thr Ser Ala Pro Thr Val Ser Val Ile Thr Ile Ser Phe Asn Asp
  1               5                  10                  15
```

```
Leu Asp Gly Leu Gln Arg Thr Val Lys Ser Val Arg Ala Gln Arg Tyr
            20                  25                  30

Arg Gly Arg Ile Glu His Ile Val Ile Asp Gly Gly Ser Gly Asp Asp
        35                  40                  45

Val Val Ala Tyr Leu Ser Gly Cys Glu Pro Gly Phe Ala Tyr Trp Gln
    50                  55                  60

Ser Glu Pro Asp Gly Gly Arg Tyr Asp Ala Met Asn Gln Gly Ile Ala
65                  70                  75                  80

His Ala Ser Gly Asp Leu Leu Trp Phe Leu His Ser Ala Asp Arg Phe
                85                  90                  95

Ser Gly Pro Asp Val Val Ala Gln Ala Val Glu Ala Leu Ser Gly Lys
            100                 105                 110

Gly Pro Val Ser Glu Leu Trp Gly Phe Gly Met Asp Arg Leu Val Gly
        115                 120                 125

Leu Asp Arg Val Arg Gly Pro Ile Pro Phe Ser Leu Arg Lys Phe Leu
    130                 135                 140

Ala Gly Lys Gln Val Val Pro His Gln Ala Ser Phe Phe Gly Ser Ser
145                 150                 155                 160

Leu Val Ala Lys Ile Gly Gly Tyr Asp Leu Asp Phe Gly Ile Ala Ala
                165                 170                 175

Asp Gln Glu Phe Ile Leu Arg Ala Ala Leu Val Cys Glu Pro Val Thr
            180                 185                 190

Ile Arg Cys Val Leu Cys Glu Phe Asp Thr Thr Gly Val Gly Ser His
        195                 200                 205

Arg Glu Pro Ser Ala Val Phe Gly Asp Leu Arg Arg Met Gly Asp Leu
    210                 215                 220

His Arg Arg Tyr Pro Phe Gly Gly Arg Arg Ile Ser His Ala Tyr Leu
225                 230                 235                 240

Arg Gly Arg Glu Phe Tyr Ala Tyr Asn Ser Arg Phe Trp Glu Asn Val
                245                 250                 255

Phe Thr Arg Met Ser Lys
            260
```

<210> 32
<211> 1023
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(1020)

<400> 32

```
gtg aag cga gcg ctc atc acc gga atc acc ggc cag gac ggc tcg tat   48
Met Lys Arg Ala Leu Ile Thr Gly Ile Thr Gly Gln Asp Gly Ser Tyr
  1               5                  10                  15

ctc gcc gaa ctg ctg ctg gcc aag ggg tat gag gtt cac ggg ctc atc   96
Leu Ala Glu Leu Leu Leu Ala Lys Gly Tyr Glu Val His Gly Leu Ile
             20                  25                  30

cgg cgc gct tcg acg ttc aac acc tcg cgg atc gat cac ctc tac gtc  144
Arg Arg Ala Ser Thr Phe Asn Thr Ser Arg Ile Asp His Leu Tyr Val
         35                  40                  45

gac ccg cac caa ccg ggc gcg cgg ctg ttt ctg cac tat ggt gac ctg  192
Asp Pro His Gln Pro Gly Ala Arg Leu Phe Leu His Tyr Gly Asp Leu
     50                  55                  60

atc gac gga acc cgg ttg gtg acc ctg ctg agc acc atc gaa ccc gac  240
Ile Asp Gly Thr Arg Leu Val Thr Leu Leu Ser Thr Ile Glu Pro Asp
 65                  70                  75                  80

gag gtg tac aac ctg gcg gcg cag tca cac gtg cgg gtg agc ttc gac  288
Glu Val Tyr Asn Leu Ala Ala Gln Ser His Val Arg Val Ser Phe Asp
                 85                  90                  95

gaa ccc gtg cac acc ggt gac acc acc ggc atg gga tcc atg cga ctg  336
Glu Pro Val His Thr Gly Asp Thr Thr Gly Met Gly Ser Met Arg Leu
            100                 105                 110

ctg gaa gcc gtt cgg ctc tct cgg gtg cac tgc cgc ttc tat cag gcg  384
Leu Glu Ala Val Arg Leu Ser Arg Val His Cys Arg Phe Tyr Gln Ala
        115                 120                 125

tcc tcg tcg gag atg ttc ggc gcc tcg ccg cca ccg cag aac gag ctg  432
Ser Ser Ser Glu Met Phe Gly Ala Ser Pro Pro Pro Gln Asn Glu Leu
    130                 135                 140

acg ccg ttc tac ccg cgg tca ccg tat ggc gcc gcc aag gtc tat tcg  480
Thr Pro Phe Tyr Pro Arg Ser Pro Tyr Gly Ala Ala Lys Val Tyr Ser
145                 150                 155                 160

tac tgg gcg acc cgc aat tat cgc gaa gcg tac gga ttg ttc gcc gtt  528
Tyr Trp Ala Thr Arg Asn Tyr Arg Glu Ala Tyr Gly Leu Phe Ala Val
                165                 170                 175

aac ggc atc ttg ttc aat cac gaa tca ccg cgg cgc ggt gag acg ttc  576
Asn Gly Ile Leu Phe Asn His Glu Ser Pro Arg Arg Gly Glu Thr Phe
            180                 185                 190

gtg acc cga aag atc acc agg gcc gtg gca cgc atc aag gcc ggt atc  624
Val Thr Arg Lys Ile Thr Arg Ala Val Ala Arg Ile Lys Ala Gly Ile
        195                 200                 205

cag tcc gag gtc tat atg ggc aat ctg gat gcg gtc cgc gac tgg ggg  672
Gln Ser Glu Val Tyr Met Gly Asn Leu Asp Ala Val Arg Asp Trp Gly
    210                 215                 220

tac gcg ccc gaa tac gtc gaa ggc atg tgg cgg atg ctg cag acc gac  720
Tyr Ala Pro Glu Tyr Val Glu Gly Met Trp Arg Met Leu Gln Thr Asp
225                 230                 235                 240
```

```
gag ccc gac gac ttc gtt ttg gcg acc ggg cgc ggt ttc acc gtg cgt   768
Glu Pro Asp Asp Phe Val Leu Ala Thr Gly Arg Gly Phe Thr Val Arg
                245                 250                 255

gag ttc gcg cgg gcc gcg ttc gag cat gcc ggt ttg gac tgg cag cag   816
Glu Phe Ala Arg Ala Ala Phe Glu His Ala Gly Leu Asp Trp Gln Gln
            260                 265                 270

tac gtg aaa ttc gac caa cgc tat ctg cgg ccc acc gag gtg gat tcg   864
Tyr Val Lys Phe Asp Gln Arg Tyr Leu Arg Pro Thr Glu Val Asp Ser
        275                 280                 285

ctg atc ggc gac gcg acc aag gct gcc gaa ttg ctg ggc tgg agg gct   912
Leu Ile Gly Asp Ala Thr Lys Ala Ala Glu Leu Leu Gly Trp Arg Ala
    290                 295                 300

tcg gtg cac act gac gag ttg gct cgg atc atg gtc gac gcg gac atg   960
Ser Val His Thr Asp Glu Leu Ala Arg Ile Met Val Asp Ala Asp Met
305                 310                 315                 320

gcg gcg ctg gag tgc gaa ggc aag ccg tgg atc gac aag ccg atg atc  1008
Ala Ala Leu Glu Cys Glu Gly Lys Pro Trp Ile Asp Lys Pro Met Ile
                325                 330                 335

gcc ggc cgg aca tga                                             1023
Ala Gly Arg Thr
            340
```

<210> 33
<211> 340
<212> PRT
<213> Mycobacterium

<400> 33

```
Met Lys Arg Ala Leu Ile Thr Gly Ile Thr Gly Gln Asp Gly Ser Tyr
  1               5                  10                  15

Leu Ala Glu Leu Leu Leu Ala Lys Gly Tyr Glu Val His Gly Leu Ile
             20                  25                  30

Arg Arg Ala Ser Thr Phe Asn Thr Ser Arg Ile Asp His Leu Tyr Val
         35                  40                  45

Asp Pro His Gln Pro Gly Ala Arg Leu Phe Leu His Tyr Gly Asp Leu
     50                  55                  60

Ile Asp Gly Thr Arg Leu Val Thr Leu Leu Ser Thr Ile Glu Pro Asp
 65                  70                  75                  80

Glu Val Tyr Asn Leu Ala Ala Gln Ser His Val Arg Val Ser Phe Asp
                 85                  90                  95

Glu Pro Val His Thr Gly Asp Thr Thr Gly Met Gly Ser Met Arg Leu
            100                 105                 110

Leu Glu Ala Val Arg Leu Ser Arg Val His Cys Arg Phe Tyr Gln Ala
        115                 120                 125

Ser Ser Ser Glu Met Phe Gly Ala Ser Pro Pro Pro Gln Asn Glu Leu
    130                 135                 140
```

```
Thr Pro Phe Tyr Pro Arg Ser Pro Tyr Gly Ala Ala Lys Val Tyr Ser
145                 150                 155                 160

Tyr Trp Ala Thr Arg Asn Tyr Arg Glu Ala Tyr Gly Leu Phe Ala Val
                165                 170                 175

Asn Gly Ile Leu Phe Asn His Glu Ser Pro Arg Arg Gly Glu Thr Phe
            180                 185                 190

Val Thr Arg Lys Ile Thr Arg Ala Val Ala Arg Ile Lys Ala Gly Ile
        195                 200                 205

Gln Ser Glu Val Tyr Met Gly Asn Leu Asp Ala Val Arg Asp Trp Gly
    210                 215                 220

Tyr Ala Pro Glu Tyr Val Glu Gly Met Trp Arg Met Leu Gln Thr Asp
225                 230                 235                 240

Glu Pro Asp Asp Phe Val Leu Ala Thr Gly Arg Gly Phe Thr Val Arg
                245                 250                 255

Glu Phe Ala Arg Ala Ala Phe Glu His Ala Gly Leu Asp Trp Gln Gln
            260                 265                 270

Tyr Val Lys Phe Asp Gln Arg Tyr Leu Arg Pro Thr Glu Val Asp Ser
        275                 280                 285

Leu Ile Gly Asp Ala Thr Lys Ala Ala Glu Leu Leu Gly Trp Arg Ala
    290                 295                 300

Ser Val His Thr Asp Glu Leu Ala Arg Ile Met Val Asp Ala Asp Met
305                 310                 315                 320

Ala Ala Leu Glu Cys Glu Gly Lys Pro Trp Ile Asp Lys Pro Met Ile
                325                 330                 335

Ala Gly Arg Thr
            340
```

<210> 34
<211> 732
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(729)

<400> 34

```
atg agg ctg gcc cgt cgc gct cgg aac atc ttg cgt cgc aac ggc atc   48
Met Arg Leu Ala Arg Arg Ala Arg Asn Ile Leu Arg Arg Asn Gly Ile
  1               5                  10                  15

gag gtg tcg cgc tac ttt gcc gaa ctg gac tgg gaa cgc aat ttc ttg   96
Glu Val Ser Arg Tyr Phe Ala Glu Leu Asp Trp Glu Arg Asn Phe Leu
             20                  25                  30
```

```
cgc caa ctg caa tcg cat cgg gtc agt gcc gtg ctc gat gtc ggg gcc   144
Arg Gln Leu Gln Ser His Arg Val Ser Ala Val Leu Asp Val Gly Ala
         35                  40                  45

aat tcg ggg cag tac gcc agg ggt ctg cgc ggc gcg ggc ttc gcg ggc   192
Asn Ser Gly Gln Tyr Ala Arg Gly Leu Arg Gly Ala Gly Phe Ala Gly
     50                  55                  60

cgc atc gtc tcg ttc gag ccg ctg ccc ggg ccc ttt gcc gtc ttg cag   240
Arg Ile Val Ser Phe Glu Pro Leu Pro Gly Pro Phe Ala Val Leu Gln
 65                  70                  75                  80

cgc agc gcc tcc acg gac ccg ttg tgg gaa tgc cgg cgc tgt gcg ctg   288
Arg Ser Ala Ser Thr Asp Pro Leu Trp Glu Cys Arg Arg Cys Ala Leu
                 85                  90                  95

ggc gat gtc gat gga acc atc tcg atc aac gtc gcc ggc aac gag ggc   336
Gly Asp Val Asp Gly Thr Ile Ser Ile Asn Val Ala Gly Asn Glu Gly
            100                 105                 110

gcc agc agt tcc gtc ttg ccg atg ttg aaa cga cat cag gac gcc ttt   384
Ala Ser Ser Ser Val Leu Pro Met Leu Lys Arg His Gln Asp Ala Phe
        115                 120                 125

cca cca gcc aac tac gtg ggc gcc caa cgg gtg ccg ata cat cga ctc   432
Pro Pro Ala Asn Tyr Val Gly Ala Gln Arg Val Pro Ile His Arg Leu
    130                 135                 140

gat tcc gtg gct gca gac gtt ctg cgg ccc aac gat att gcg ttc ttg   480
Asp Ser Val Ala Ala Asp Val Leu Arg Pro Asn Asp Ile Ala Phe Leu
145                 150                 155                 160

aag atc gac gtt caa gga ttc gag aag cag gtg atc gcg ggt ggc gat   528
Lys Ile Asp Val Gln Gly Phe Glu Lys Gln Val Ile Ala Gly Gly Asp
                165                 170                 175

tca acg gtg cac gac cga tgc gtc ggc atg cag ctc gag ctg tct ttc   576
Ser Thr Val His Asp Arg Cys Val Gly Met Gln Leu Glu Leu Ser Phe
            180                 185                 190

cag ccg ttg tac gag ggt ggc atg ctc atc cgc gag gcg ctc gat ctc   624
Gln Pro Leu Tyr Glu Gly Gly Met Leu Ile Arg Glu Ala Leu Asp Leu
        195                 200                 205

gtg gat tcg ttg ggc ttt acg ctc tcg gga ttg caa ccc ggt ttc acc   672
Val Asp Ser Leu Gly Phe Thr Leu Ser Gly Leu Gln Pro Gly Phe Thr
    210                 215                 220

gac ccc cgc aac ggt cga atg ctg cag gcc gat ggc atc ttc ttc cgg   720
Asp Pro Arg Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg
225                 230                 235                 240

ggc agc gat tga                                                  732
Gly Ser Asp
```

<210> 35
<211> 243
<212> PRT
<213> Mycobacterium

<400> 35

```
Met Arg Leu Ala Arg Arg Ala Arg Asn Ile Leu Arg Arg Asn Gly Ile
  1               5                  10                  15

Glu Val Ser Arg Tyr Phe Ala Glu Leu Asp Trp Glu Arg Asn Phe Leu
             20                  25                  30

Arg Gln Leu Gln Ser His Arg Val Ser Ala Val Leu Asp Val Gly Ala
         35                  40                  45

Asn Ser Gly Gln Tyr Ala Arg Gly Leu Arg Gly Ala Gly Phe Ala Gly
     50                  55                  60

Arg Ile Val Ser Phe Glu Pro Leu Pro Gly Pro Phe Ala Val Leu Gln
 65                  70                  75                  80

Arg Ser Ala Ser Thr Asp Pro Leu Trp Glu Cys Arg Arg Cys Ala Leu
                 85                  90                  95

Gly Asp Val Asp Gly Thr Ile Ser Ile Asn Val Ala Gly Asn Glu Gly
            100                 105                 110

Ala Ser Ser Ser Val Leu Pro Met Leu Lys Arg His Gln Asp Ala Phe
        115                 120                 125

Pro Pro Ala Asn Tyr Val Gly Ala Gln Arg Val Pro Ile His Arg Leu
    130                 135                 140

Asp Ser Val Ala Ala Asp Val Leu Arg Pro Asn Asp Ile Ala Phe Leu
145                 150                 155                 160

Lys Ile Asp Val Gln Gly Phe Glu Lys Gln Val Ile Ala Gly Gly Asp
                165                 170                 175

Ser Thr Val His Asp Arg Cys Val Gly Met Gln Leu Glu Leu Ser Phe
            180                 185                 190

Gln Pro Leu Tyr Glu Gly Gly Met Leu Ile Arg Glu Ala Leu Asp Leu
        195                 200                 205

Val Asp Ser Leu Gly Phe Thr Leu Ser Gly Leu Gln Pro Gly Phe Thr
    210                 215                 220

Asp Pro Arg Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg
225                 230                 235                 240

Gly Ser Asp
```

<210> 36
<211> 732
<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(729)

<400> 36

```
gtg aaa tcg ttg aaa ctc gct cgt ttc atc gcg cgt agc gcc gcc ttc   48
Met Lys Ser Leu Lys Leu Ala Arg Phe Ile Ala Arg Ser Ala Ala Phe
  1               5                  10                  15

gag gtt tcg cgc cgc tat tct gag cga gac ctg aag cac cag ttt gtg   96
Glu Val Ser Arg Arg Tyr Ser Glu Arg Asp Leu Lys His Gln Phe Val
            20                  25                  30

aag caa ctc aaa tcg cgt cgg gta gat gtc gtt ttc gat gtc ggc gcc   144
Lys Gln Leu Lys Ser Arg Arg Val Asp Val Val Phe Asp Val Gly Ala
        35                  40                  45

aac tca gga caa tac gcc gcc ggc ctc cgc cga gca gca tat aag ggc   192
Asn Ser Gly Gln Tyr Ala Ala Gly Leu Arg Arg Ala Ala Tyr Lys Gly
    50                  55                  60

cgc att gtc tcg ttc gaa ccg cta tcc gga ccg ttt acg atc ttg gaa   240
Arg Ile Val Ser Phe Glu Pro Leu Ser Gly Pro Phe Thr Ile Leu Glu
65                  70                  75                  80

agc aaa gcg tca acg gat cca ctt tgg gat tgc cgg cag cat gcg ttg   288
Ser Lys Ala Ser Thr Asp Pro Leu Trp Asp Cys Arg Gln His Ala Leu
                85                  90                  95

ggc gat tct gat gga acg gtt acg atc aat atc gca gga aac gcc ggt   336
Gly Asp Ser Asp Gly Thr Val Thr Ile Asn Ile Ala Gly Asn Ala Gly
            100                 105                 110

cag agc agt tcc gtc ttg ccc atg ctg aaa agt cat cag aac gct ttt   384
Gln Ser Ser Ser Val Leu Pro Met Leu Lys Ser His Gln Asn Ala Phe
        115                 120                 125

ccc ccg gca aac tat gtc ggt acc caa gag gcg tcc ata cat cga ctt   432
Pro Pro Ala Asn Tyr Val Gly Thr Gln Glu Ala Ser Ile His Arg Leu
    130                 135                 140

gat tcc gtg gcg cca gaa ttt cta ggc atg aac ggt gtc gct ttt ctc   480
Asp Ser Val Ala Pro Glu Phe Leu Gly Met Asn Gly Val Ala Phe Leu
145                 150                 155                 160

aag gtc gac gtt caa ggc ttt gaa aag cag gtg ctc gcc ggg ggc aaa   528
Lys Val Asp Val Gln Gly Phe Glu Lys Gln Val Leu Ala Gly Gly Lys
                165                 170                 175

tca acc ata gat gac cat tgc gtc ggc atg caa ctc gaa ctg tcc ttc   576
Ser Thr Ile Asp Asp His Cys Val Gly Met Gln Leu Glu Leu Ser Phe
            180                 185                 190

ctg ccg ttg tac gaa ggt ggc atg ctc att cct gaa gcc ctc gat ctc   624
Leu Pro Leu Tyr Glu Gly Gly Met Leu Ile Pro Glu Ala Leu Asp Leu
        195                 200                 205

gtg tat tcc ttg ggc ttc acg ttg acg gga ttg ctg cct tgt ttc att   672
Val Tyr Ser Leu Gly Phe Thr Leu Thr Gly Leu Leu Pro Cys Phe Ile
    210                 215                 220

gat gca aat aat ggt cga atg ttg cag gcc gac ggc atc ttt ttc cgc   720
Asp Ala Asn Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg
225                 230                 235                 240
```

gag gac gat tga 732
Glu Asp Asp

<210> 37
<211> 243
<212> PRT
<213> Mycobacterium

<400> 37
Met Lys Ser Leu Lys Leu Ala Arg Phe Ile Ala Arg Ser Ala Ala Phe
1 5 10 15

Glu Val Ser Arg Arg Tyr Ser Glu Arg Asp Leu Lys His Gln Phe Val
20 25 30

Lys Gln Leu Lys Ser Arg Arg Val Asp Val Val Phe Asp Val Gly Ala
35 40 45

Asn Ser Gly Gln Tyr Ala Ala Gly Leu Arg Arg Ala Ala Tyr Lys Gly
50 55 60

Arg Ile Val Ser Phe Glu Pro Leu Ser Gly Pro Phe Thr Ile Leu Glu
65 70 75 80

Ser Lys Ala Ser Thr Asp Pro Leu Trp Asp Cys Arg Gln His Ala Leu
85 90 95

Gly Asp Ser Asp Gly Thr Val Thr Ile Asn Ile Ala Gly Asn Ala Gly
100 105 110

Gln Ser Ser Ser Val Leu Pro Met Leu Lys Ser His Gln Asn Ala Phe
115 120 125

Pro Pro Ala Asn Tyr Val Gly Thr Gln Glu Ala Ser Ile His Arg Leu
130 135 140

Asp Ser Val Ala Pro Glu Phe Leu Gly Met Asn Gly Val Ala Phe Leu
145 150 155 160

Lys Val Asp Val Gln Gly Phe Glu Lys Gln Val Leu Ala Gly Gly Lys
165 170 175

Ser Thr Ile Asp Asp His Cys Val Gly Met Gln Leu Glu Leu Ser Phe
180 185 190

Leu Pro Leu Tyr Glu Gly Gly Met Leu Ile Pro Glu Ala Leu Asp Leu
195 200 205

Val Tyr Ser Leu Gly Phe Thr Leu Thr Gly Leu Leu Pro Cys Phe Ile
210 215 220

Asp Ala Asn Asn Gly Arg Met Leu Gln Ala Asp Gly Ile Phe Phe Arg
225 230 235 240

Glu Asp Asp

<210> 38
<211> 828

<212> DNA
<213> Mycobacterium

<220>
<221> CDS
<222> (1)..(825)

<400> 38

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atg gtg cag acg aaa cga tac gcc ggc ttg acc gca gct aac aca aag   48
Met Val Gln Thr Lys Arg Tyr Ala Gly Leu Thr Ala Ala Asn Thr Lys
  1               5                  10                  15

aaa gtc gcc atg gcc gca cca atg ttt tcg atc atc atc ccc acc ttg   96
Lys Val Ala Met Ala Ala Pro Met Phe Ser Ile Ile Ile Pro Thr Leu
            20                  25                  30

aac gtg gct gcg gta ttg cct gcc tgc ctc gac agc atc gcc cgt cag   144
Asn Val Ala Ala Val Leu Pro Ala Cys Leu Asp Ser Ile Ala Arg Gln
         35                  40                  45

acc tgc ggt gac ttc gag ctg gta ctg gtc gac ggc ggc tcg acg gac   192
Thr Cys Gly Asp Phe Glu Leu Val Leu Val Asp Gly Gly Ser Thr Asp
     50                  55                  60

gaa acc ctc gac atc gcc aac att ttc gcc ccc aac ctc ggc gag cgg   240
Glu Thr Leu Asp Ile Ala Asn Ile Phe Ala Pro Asn Leu Gly Glu Arg
 65                  70                  75                  80

ttg atc att cat cgc gac acc gac cag ggc gtc tac gac gcc atg aac   288
Leu Ile Ile His Arg Asp Thr Asp Gln Gly Val Tyr Asp Ala Met Asn
                85                  90                  95

cgc ggc gtg gac ctg gcc acc gga acg tgg ttg ctc ttt ctg ggc gcg   336
Arg Gly Val Asp Leu Ala Thr Gly Thr Trp Leu Leu Phe Leu Gly Ala
            100                 105                 110

gac gac agc ctg tac gag gct gac acc ctg gcg cgg gtg gcc gcc ttc   384
Asp Asp Ser Leu Tyr Glu Ala Asp Thr Leu Ala Arg Val Ala Ala Phe
        115                 120                 125

att ggc gaa cac gag ccc agc gat ctg gta tat ggc gac gtg atc atg   432
Ile Gly Glu His Glu Pro Ser Asp Leu Val Tyr Gly Asp Val Ile Met
    130                 135                 140

cgc tca acc aat ttc cgc tgg ggt ggc gcc ttc gac ctc gac cgt ctg   480
Arg Ser Thr Asn Phe Arg Trp Gly Gly Ala Phe Asp Leu Asp Arg Leu
145                 150                 155                 160

ttg ttc aag cgc aac atc tgc cat cag gcg atc ttc tac cgc cgc gga   528
Leu Phe Lys Arg Asn Ile Cys His Gln Ala Ile Phe Tyr Arg Arg Gly
                165                 170                 175

ctc ttc ggc acc atc ggt ccc tac aac ctc cgc tac cgg gtc ctg gcc   576
Leu Phe Gly Thr Ile Gly Pro Tyr Asn Leu Arg Tyr Arg Val Leu Ala
            180                 185                 190

gac tgg gac ttc aat att cgc tgc ttt tcc aac cca gcg ctc gtc acc   624
Asp Trp Asp Phe Asn Ile Arg Cys Phe Ser Asn Pro Ala Leu Val Thr
        195                 200                 205
```

```
cgc tac atg cac gtg gtc gtt gca agc tac aac gaa ttc ggc ggg ctc   672
Arg Tyr Met His Val Val Val Ala Ser Tyr Asn Glu Phe Gly Gly Leu
    210                 215                 220

agc aat acg atc gtc gac aag gag ttt ttg aag cgg ctg ccg atg tcc   720
Ser Asn Thr Ile Val Asp Lys Glu Phe Leu Lys Arg Leu Pro Met Ser
225                 230                 235                 240

acg aga ctc ggc ata agg ctg gtc ata gtt ctg gtg cgc agg tgg cca   768
Thr Arg Leu Gly Ile Arg Leu Val Ile Val Leu Val Arg Arg Trp Pro
                245                 250                 255

aag gtg atc agc agg gcc atg gta atg cgc acc gtc att tct tgg cgg   816
Lys Val Ile Ser Arg Ala Met Val Met Arg Thr Val Ile Ser Trp Arg
            260                 265                 270

cgc cga cgt tag                                                  828
Arg Arg Arg
        275
```

<210> 39
<211> 275
<212> PRT
<213> Mycobacterium

<400> 39

```
Met Val Gln Thr Lys Arg Tyr Ala Gly Leu Thr Ala Ala Asn Thr Lys
  1               5                  10                  15

Lys Val Ala Met Ala Ala Pro Met Phe Ser Ile Ile Ile Pro Thr Leu
             20                  25                  30

Asn Val Ala Ala Val Leu Pro Ala Cys Leu Asp Ser Ile Ala Arg Gln
         35                  40                  45

Thr Cys Gly Asp Phe Glu Leu Val Leu Val Asp Gly Gly Ser Thr Asp
     50                  55                  60

Glu Thr Leu Asp Ile Ala Asn Ile Phe Ala Pro Asn Leu Gly Glu Arg
 65                  70                  75                  80

Leu Ile Ile His Arg Asp Thr Asp Gln Gly Val Tyr Asp Ala Met Asn
                 85                  90                  95

Arg Gly Val Asp Leu Ala Thr Gly Thr Trp Leu Leu Phe Leu Gly Ala
            100                 105                 110

Asp Asp Ser Leu Tyr Glu Ala Asp Thr Leu Ala Arg Val Ala Ala Phe
        115                 120                 125

Ile Gly Glu His Glu Pro Ser Asp Leu Val Tyr Gly Asp Val Ile Met
    130                 135                 140

Arg Ser Thr Asn Phe Arg Trp Gly Gly Ala Phe Asp Leu Asp Arg Leu
145                 150                 155                 160

Leu Phe Lys Arg Asn Ile Cys His Gln Ala Ile Phe Tyr Arg Arg Gly
                165                 170                 175
```

Leu Phe Gly Thr Ile Gly Pro Tyr Asn Leu Arg Tyr Arg Val Leu Ala
180 185 190

Asp Trp Asp Phe Asn Ile Arg Cys Phe Ser Asn Pro Ala Leu Val Thr
195 200 205

Arg Tyr Met His Val Val Val Ala Ser Tyr Asn Glu Phe Gly Gly Leu
210 215 220

Ser Asn Thr Ile Val Asp Lys Glu Phe Leu Lys Arg Leu Pro Met Ser
225 230 235 240

Thr Arg Leu Gly Ile Arg Leu Val Ile Val Leu Val Arg Arg Trp Pro
245 250 255

Lys Val Ile Ser Arg Ala Met Val Met Arg Thr Val Ile Ser Trp Arg
260 265 270

Arg Arg Arg
275

<210> 40
<211> 24
<212> DNA
<213> Mycobacterium

<400> 40
gatgccgtga ggaggtaaag ctgc 24

<210> 41
<211> 24
<212> DNA
<213> Mycobacterium

<400> 41
gatacggctc ttgaatcctg cacg 24